JAMES & ESTHER KING BIOMEDICAL RESEARCH PROGRAM

2009 Annual Report

The James & Esther King Biomedical Research Program

The five long-term goals of the Program are to:

1. Improve the health of Floridians by researching better prevention, diagnoses, treatments, and cures for cancer, cardiovascular disease, stroke, and pulmonary disease.

2. Expand the foundation of biomedical knowledge relating to the prevention, diagnosis, treatment, and cure of diseases related to tobacco use including cancer, cardiovascular disease, stroke, and pulmonary disease.

3. Improve the quality of the state's academic health centers by bringing the advances of biomedical research into the training of physicians and other healthcare providers.

4. Increase the state's per capita funding for research by undertaking new initiatives in public health and biomedical research that will attract additional funding from outside the state.

5. Stimulate economic activity in the state in areas related to biomedical research including the research and production of pharmaceuticals, biotechnology, and medical devices.

The James & Esther King Biomedical Research Program garnered national recognition from the State Science and Technology Institute (SSTI) as the winner of its 2009 Excellence in Tech-based Economic Development (TBED) Award in the category of expanding research infrastructure. Department of Health officials accepted the award, pictured on the cover, at SSTI's 13th Annual Conference in Overland Park, Kansas, on October 22, 2009.

The report does not necessarily reflect the opinions of the Florida Department of Health or its staff, and any recommendations contained within are those of the Program's Advisory Council.

For more information or to request additional copies of this report, please contact Florida Biomedical Research Programs in the Office of Public Health Research, (850) 245-4585. To download a copy of this and prior years' reports, go to www.floridabiomed.com.

The Honorable Charlie Crist, Governor
The Honorable Jeff Atwater, Senate President
The Honorable Larry Cretul, House Speaker
Ana M. Viamonte Ros, M.D., M.P.H., State Surgeon General, Florida Department of Health

Dear Governor Crist, President Atwater, Speaker Cretul, and Surgeon General Viamonte Ros:

Ten years ago, Florida made a strategic commitment to leadership in the field of tobacco-related disease research. The James & Esther King Program is a direct outgrowth of that commitment, and it shares the state's vision of improving Florida's physical and fiscal health by advancing new approaches to prevent, diagnose and treat tobacco-related disease. In its first decade, the Program has made consistent and substantive progress towards its goals by funding innovative research, supporting and expanding Florida's biomedical research community, and facilitating productive collaboration between the state's academic research centers and private biomedical industry.

The 2009 James & Esther King Biomedical Research Program Annual Report summarizes the organization's achievements over its first ten years. As proud as I am of what we have accomplished to date, I have great excitement and enthusiasm at the Program's prospects for continued success and even greater impact in the future. The Legislature's decision to allocate 2.5 percent of the proceeds from an increase in the cigarette tax to fund the Program substantially increases our financial resources, enabling us to provide increased funding for tobacco-related disease research throughout the state. On behalf of Florida's biomedical research community, we deeply appreciate this increased level of support, especially at this time of economic difficulty.

Through ongoing evaluation and analysis, the Program has clear ideas on how to make the most effective use of the funds we receive from the state. Continued support of investigators at the cutting edge of tobacco-related disease research is essential to improving the health of Florida's citizens.

Providing grant recipients with mentoring opportunities, objective evaluation of their work, and critical financial support positions them to compete successfully for federal research grants, thereby leveraging the state investment and increasing Florida's per capita funding.

Fostering collaborations that translate promising science into commercial opportunities strengthens the state's position as a leading biomedical research community. It also stimulates economic activity by helping start-up biotechnology and pharmaceutical ventures become successful companies that offer high-quality jobs to Floridians.

We are grateful that the Senate's statutory review resulted in a recommendation to re-enact the legislation that brought the James & Esther King Program into existence. This recommendation is a vote of confidence in the Program's historic performance and future potential. I hope that each of you will do your part to ensure passage of the legislation upon which the future of the Program rests.

Tobacco-related diseases continue to exact a tremendous toll from Floridians and from the state. We recognize that the increased funding recently provided to the Program is as much a reflection of our achievements as it is recognition of the research challenges that lie ahead. I have every confidence that the James & Esther King Program will build on its first decade of success and will continue as a valuable component of Florida's biomedical investment strategy. Thank you for your support.

Sincerely,

Richard J. Bookman, Ph.D.
Chair, Florida Biomedical Research Council

Honoring the Memory of Senator Jim King

Photo: Associated Press

After more than two decades of public service, Senator James E. "Jim" King of Jacksonville passed away July 26th after a battle with cancer. Among Senator King's many accomplishments as a long-time and esteemed member of Florida's legislature, his support for Florida's biomedical research enterprise is what many consider his most valuable contribution to the citizens of Florida.

In 1999 as a freshman senator, King introduced Senate Bill 2558 that led to the creation of the Florida Biomedical Research Program, the state's first major investment in accelerating progress towards the prevention, diagnosis, treatment, and cure of diseases related to tobacco use. The Program received financial support through direct annual appropriations as well as the Lawton Chiles Endowment Fund, established with the 1997 Florida tobacco settlement agreement. A few years later, in part as a result of his continued support for the growth of the Program, the Senate renamed it the James & Esther King Biomedical Research Program in honor of his parents, both victims of tobacco-related cancer.

As the James & Esther King Program became an increasingly important factor in the state's biomedical research enterprise, Senator King remained one of the Program's most ardent champions. His leadership undoubtedly contributed to a snowball effect for increased state support of biomedical research and biotechnology culminating with the 2009 passage of the cigarette surcharge increase. This law directs up to $50 million dollars to be shared equally between the King Program and the Bankhead-Coley Cancer Research Program. The latter was created in 2006 to advance progress towards cures for cancer.

Senator King's support for research was so singular that Governor Charlie Crist recognized it when remembering King's life: "Jim leaves a great legacy of service—including his significant efforts to promote biomedical research to find cures for the horrible diseases that bring suffering to so many Floridians."

Dr. Richard Bookman, Chair of the Florida Biomedical Research Advisory Council, recounts Senator King's contributions to the Program: "Senator King provided visionary leadership to support the growth of biomedical research in Florida. He saw so clearly that the search for cures was a triple benefit: a beacon of hope for those afflicted, an investment in human capital advancing our understanding, and a bet on Florida's role as a leader in our nation. We will all miss his warmth and his passionate and outspoken support for doing the right thing."

King's leadership and vision will be long remembered in the Florida biomedical research and healthcare community.

To read more about Senator King, see http://www.jacksonville.com/news/metro/2009-07-26/story/state_sen_jim_king_dies_after_battle_with_pancreatic_cancer.

James and Esther King Biomedical Research Program

Annual Report
January–December 2009

Submitted to

The Governor
The President of the Senate
The Speaker of the House of Representatives
The Surgeon General
State of Florida

and

The Florida Center for Universal Research to Eradicate Disease

by

Dr. Richard Bookman, Chair
Biomedical Research Advisory Council

February 1, 2010

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Executive Summary

For ten years, the James & Esther King Biomedical Research Program (Program) has been an integral component of Florida's effort to address the tremendous health and financial challenges resulting from tobacco-related diseases. In its first decade, the Program awarded 188 grants totaling $79.2 million in a diverse portfolio of projects. Because of the significant increase in program appropriations for fiscal year 2009-10, nearly a quarter of these awards were made in 2009. Consequently, Florida's investment in the Program can be expected to produce significantly greater dividends in the decade to come.

This annual report presents the 45 new grants awarded in 2009. More importantly, it documents Program achievements in accelerating the prevention, diagnosis, treatment, and cure of diseases related to tobacco while also stimulating the growth of Florida's technology-based economy.

One important accomplishment is the attraction of additional external funding. James & Esther King grantees obtained nearly $37 million in external funding this year, representing a 41 percent increase from last year's cumulative total. Since 1999, Florida's share of research grant funding from the National Institutes of Health has climbed from 21st in the nation to 17th.

Other important measures of success are publications in peer-reviewed journals and invited presentations at scientific meetings. Both provide evidence of the national and international importance of the findings generated by the Program's grant recipients. Since Program inception, publications by King grantees reached 362 this year and cumulative number of presentations totaled 906.

In addition, the Program is increasing Florida's biomedical research capacity by helping build a highly skilled, well-trained workforce. More than 220 scientists at 16 different institutions throughout the state have led Program projects, aided by hundreds more graduate and post-doctoral students and laboratory personnel.

Program at a Glance

The James & Esther King Program offers competitive tobacco-related research grants to Florida institutions based on scientific merit. The Program is funded by 2.5 percent (up to $25 million) of proceeds from the state cigarette surcharge plus a portion of interest earnings from the Lawton Chiles Endowment Fund, established with monies received from Florida's legal settlement with the tobacco industry. The Program is managed by the Florida Department of Health and 11-member Advisory Council.

The Program's track record of success has garnered favorable attention both within and outside Florida. In 2009, the Program received a national award for Excellence in Technology Based Economic Development from the State Science and Technology Institute as a model for increasing research infrastructure. Recognition has also come from the National Cancer Institute (NCI). Based on NCI's endorsement of the peer review and funding decision processes used to select James & Esther King and Bankhead-Coley awards, Florida joins one other state with competitive grant programs to receive this endorsement. This means that these grants are offering an important advantage to Florida's cancer centers in securing large, highly competitive NCI grants, including the H. Lee Moffitt Cancer Center & Research Institute, the Sylvester Cancer Center, and the University of Florida Shands Cancer Center.

Despite continued support and recognition for the Program, the downturn in Florida's economic cycle forced a 25 percent reduction in the Program's fiscal year (FY) 2008-2009 appropriations. Consequently, in January 2009, the Program responded by trimming administrative expenses and reducing current-year grants. Four months

June 2001 First Awards Made

$79.2 million Total Value of Awards

$127 million Additional Funding Leveraged

188 No. of Awards Made

16 No. of Florida Institutions Supported

906 No. of Invited Presentations at Scientific Meetings

362 No. of Publications Generated

later, the Legislature increased the FY 2009-2010 Program budget more than twofold with up to $25 million of the newly increased state cigarette surcharge.

As a result of this funding increase, the Program restored previous reductions and awarded grants in two competitions during 2009. In the first round, 25 awards totaling $10 million were made for projects beginning July 1. The second round expanded the types of grants offered this year, and resulted in 20 awards valued at $10.5 million for projects beginning January 1, 2010. Twelve Florida institutions were beneficiaries of Program grants in 2009.

The increase in funding led the Program to undertake the development of a new strategic plan. The process began with a series of discussions involving Florida stakeholders and national leaders in biomedical research to help define major funding trends, best practices, and special needs in order to establish a planning framework. At a special November meeting, the Florida Biomedical Research Advisory Council prioritized needs and opportunities and began crafting a new five-year plan to direct Program growth and set its course for 2010 and beyond.

The Program is currently undergoing a Legislative sunset review, as its enabling legislation is due to expire in 2010. Last summer, the Senate committee that evaluated the Program against its statutory goals recommended re-enactment. This endorsement reflects the important role that the Program plays in helping Florida improve the health of the state's citizens while also stimulating its technology-based economy.

Tobacco-related diseases continue to reduce longevity and quality of life for too many of Florida's citizens. The awards granted in the Program's first ten years have helped to accelerate the development of novel prevention, diagnostic, and therapeutic approaches to address those challenges. The Program's strategies for critical selection of grant applications, ongoing oversight of funded research, and diligent management of its financial resources over the past decade have provided a foundation of success and create a platform for continued progress toward achieving its goals.

Background

A Commitment to Addressing the Challenges of Tobacco-Related Disease

Ten years ago, Florida made a commitment to address the challenges of tobacco-related disease within the state. This was a natural outgrowth of Florida's leadership in tobacco litigation, which resulted in a landmark settlement with Big Tobacco in 1997. Florida dedicated a portion of its settlement funds to support tobacco-related disease research, setting the money aside in the Lawton Chiles Endowment Fund. In 1999, the Legislature established the Florida Biomedical Research Program to provide perpetual funding to support research addressing Florida's health issues in the areas of tobacco-related cancer, cardiovascular disease, stroke, and pulmonary disease, as well as in behavioral research targeting prevention of disease stemming from tobacco use. The Program was renamed the James & Esther King Biomedical Research Program (hereafter called the "Program") in 2003.

Through the Program, Florida has made a significant financial commitment to tobacco-related research over the past decade – nearly $80 million since 2001, when the first grants were awarded. This commitment was strengthened in FY 2009-2010, when the Legislature allocated 2.5 percent, up to $25 million annually, of the proceeds from an increase in tobacco surcharges to the Program. This allocation substantially increases the Program's financial resources as it moves into its second decade.

Stable financial support is essential for achieving the Program's objectives of supporting research that enhances the prevention, diagnosis, treatment, and cure of tobacco-related disease; bringing advances in biomedical science into the training of physicians and healthcare providers; and undertaking new initiatives in biomedical research that will attract additional funding and stimulate economic activity.

1999

Program Authorized by Florida Legislature

The Florida Legislature created the Florida Biomedical Trust Fund (section (s.) 215.5601, *Florida Statutes (F.S.)* and the Florida Biomedical Research Program (s.) 215.5602, *F.S.* (located in Appendix A).

Investment earnings from a portion of the $150 million set aside in the Lawton Chiles Endowment Fund (LCEF) were marked exclusively for funding research initiatives into the prevention, diagnosis, treatment, and cure of tobacco-related diseases such as cancer, cardiovascular disease, stroke, and pulmonary disease.

2001

Initial Grants Awarded

Forty-two inaugural grants totaling $16.45 million were awarded; these multi-year grants were sustained with State appropriations in 2002 and 2003.

2003

Funding Limited to Existing Grants

The Legislature appropriated money for existing grants only, which threatened the Program with a loss of credibility in the scientific community. Three one-year grants totaling $150,000 were made using funds allotted for Program administrative costs.

Responding to the FY 2009-2010 Budget Increase

In light of the additional resources that became available to the Program beginning this fiscal year, the Program offered two rounds of funding in FY 2009-2010. The spring competition that constitutes the Program's normal funding cycle led to awards that began in July. Rather than lower its standards for scientific merit by funding more applications from this same competition, the Program released three Special Calls for Grant Applications in August for awards to begin in January 2010. These Special Calls expanded the means of support that the Program provides to investigators engaged in tobacco-related disease research. A more detailed discussion of the outcome of both competitions is provided in the 2009 Grant Awards section.

Helping Build the Future of Florida's Biomedical Research Community

With a decade of achievement behind it, and dedicated funding in the years ahead, the Program is well positioned to continue providing superior returns on Florida's investment.

- The funded projects represent the most promising research across the state to improve the prevention, diagnosis, treatment, and cure of tobacco-related diseases, thus helping to address critical health challenges within Florida.

- The Program's grants enhance Florida's position as a leader in tobacco-related biomedical research, and support the state's ongoing efforts to create a stable academic environment that helps to attract and retain top researchers and high-quality jobs.

Stable Funding Base Created

The Florida Legislature allowed annual appropriation balances from the Biomedical Research Trust Fund to be expended over a period of three years. This decision protected the completion of existing grant awards, allowed for the continuity of multi-year research, and created a more stable and sustainable funding base.

2004 **2006** **2009**

Extended Support Authorized

The Florida Legislature appropriated general revenue funds of $6 million (in addition to the interest earnings from the LCEF) annually for five years to the Program, at which time the Legislature would review the Program's performance, outcomes, and financial management.

Budget Changes

The Florida Legislature raised the funding level up to $25 million annually by allocating 2.5 percent of the proceeds from an increase in tobacco surcharges to fund the Program.

- Grants support the state's economy by providing dollars to researchers in Florida and by enabling investigators to compete more successfully for follow-on funding from external sources, such as National Institutes of Health (NIH), that bring additional research dollars into the state.

- The Program holds its grant recipients accountable for using their awards effectively, which helps to improve the state's return on its investments.

Taken together, these benefits position the Program as a strategic component of Florida's overall biomedical investment portfolio.

A brief description of all grant types, or mechanisms, offered through the Program since its inception is provided for reference in Table 1.

Providing Critical Support to Technology Development and Commercialization

The Program dovetails with larger efforts to stimulate Florida's economy for the long term. The 2009 Task Force on the Study of Biotech Competitiveness was created by the 2007 Florida Legislature to study economic policies necessary for "securing Florida's competitive edge in the growing biotech sector."[1] Reflecting the Program's value in creating opportunities for economic growth, the first item on the list of Task Force recommendations to create a successful entrepreneurial climate is sustained funding for Florida's Biomedical Research Programs: the James & Esther King Biomedical Research Program and the Bankhead-Coley Cancer Research Program.

The 2009 award from the State Science and Technology Institute represents a third party national endorsement of the Program's innovative role in increasing research infrastructure, specifically as it relates to technology-based economic development. According to Dan Berglund, SSTI President and CEO, awards recognize organizations that "serve as best practice models in the field for their demonstrated leadership and meaningful impact to state and regional economies."

Positioned For Success in the Next Ten Years

The Florida Legislature is required by statute to review the Program's performance during the 2010 regular legislative session. In the summer of 2009, the Senate Committee on Health Care Regulation reviewed the Program's performance, outcomes, and financial management. Based on the Program's achievements, the committee recommended that the Senate re-enact the legislation that created the Program.

The Program has developed systems, policies, and procedures that are proving to be easily expanded to process and evaluate a greater volume of applications and manage a larger portfolio of grants. It has matured in its use of self-evaluation tools and performance metrics to fine-tune operations and measure progress.

With an eye on the future, the Florida Biomedical Research Advisory Council ("Advisory Council") and the Florida Department of Health began a rigorous strategic planning process in late 2009 that will shape Program direction in 2010 and beyond. More information about this effort can be found in the "Planning for the Future" section.

Table 1 – Program Grant Mechanisms Offered Since Program Inception

Investigator Initiated Research (IIR) Grants: Fund research for Florida investigators at all experience levels on a wide variety of tobacco-related research topics (Offered in 2001)
New Investigator Research (NIR) Grants: Provide support to Florida-based investigators starting independent research careers in tobacco-related projects, completed under the guidance of an experienced Florida mentor (Offered 2001 and 2004-2009)
Small Business Technology Transfer (SBTT) and Technology Transfer/Commercialization Partnership (TTCP) Grants: Fund collaborations between academic researchers and small, Florida-based biomedical businesses to translate discoveries into new products and therapies (Offered 2004-2007 and 2009)
Team Science Program (TSP) Grants: Foster collaboration among three to five Florida researchers, supporting complex projects with the potential to secure large external grants (Offered 2004-2009)
Bridge Grants: Provide one year of interim support for tobacco-related research projects receiving high scores in federal competitions that were not funded due to Federal budget constraints (Offered 2008-2009)
Florida Research Challenge (RC1) Grants: Provide support for high-risk, high-reward tobacco-related research projects submitted by Florida researchers in response to NIH's 2009 Challenge Grant competition and not funded due to Federal budget constraints (Offered in Fall 2009 to begin January 2010)
Shared Instrument Grants (SIG): Improve access to state-of-the-art research instruments that can only be justified on a shared-use basis (Offered in Fall 2009 to begin January 2010)

Program Accomplishments

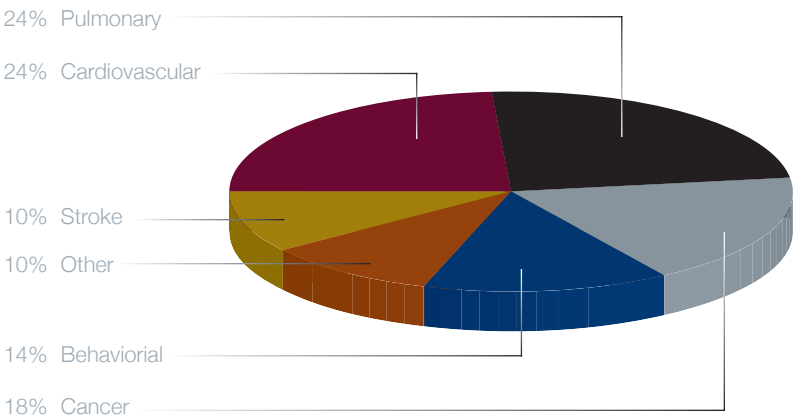


Figure 1 – Grant Portfolio by Area of Focus

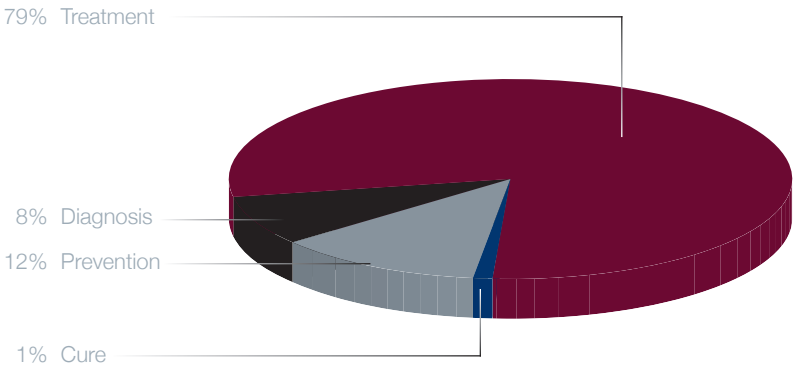


Figure 2 – Grant Portfolio by Research Objective

The following sections provide a brief summary of cumulative King Program accomplishments to date and the new grants awarded in 2009.

A Decade of Achievement

One of the Program's strategic commitments is nurturing a new generation of investigators. Key to realizing this commitment is supporting new research projects that have the potential to both launch a career and shed new light on tobacco-related disease processes. In addition, Program grants have enabled sustained funding and research momentum for established investigators, allowing them to generate compelling data and merit longer-term funding from other sources. Since its inception in 1999, the Program has provided 188 grants to Florida-based researchers, totaling $79.2 million. So far, 71 out of 90 completed projects funded by the Program have received follow-on support from external sources.

As the number of Program grants in the state increases, the state's biomedical knowledge base grows, evidenced by 906 scientific presentations and 362 publications in peer-reviewed journals generated by Program Grantees. Appendix B lists publications reported by grantees in 2009.

Figures 1 and 2 depict the allocation of the Program's cumulative grant portfolio by disease area and research objective, demonstrating that the Program has established a diversified portfolio of tobacco-related research grants.

Stimulating Tobacco-Related Research at Academic Health Centers

The Program's grants have served as a catalyst for the establishment and growth of tobacco-related research programs at several of the state's academic health centers. New research activity at health centers has in turn spawned the recruitment and training of physician-scientists. (See the Pulmonary and Cancer sections "Behind the Numbers.") Since 2001, the Program has funded 37 researchers with M.D. degrees and 18 with M.D. and Ph.D. degrees out of a total of 188 funded principal investigators. Funding researchers who have clinical expertise and responsibilities is critical to the Program's goal of integrating biomedical research with the training of physicians and other healthcare providers. These investigators help to bring laboratory insights into clinical practice and also utilize their clinical experience to identify unmet medical needs, tailoring research projects to address specific clinical challenges.

Enhancing Florida's Economic Prospects

Expanding the state's tobacco-related research programs benefits the entire biomedical research community as well as Florida's overall economy. Beyond funding a specific investigator or research program, Program awards may also enable recipients to hire additional personnel within their laboratories, creating new jobs. Innovative scientific ideas may have commercial potential that leads to collaboration between the academic and commercial research communities. In supporting research and providing grants that facilitate these partnerships, the Program's funds enhance technology transfer activities, increasing the likelihood that new biomedical companies will establish a base in Florida. Each of these start-up companies is an engine for creating new jobs and stimulating additional economic activity. To date, investigators supported by the Program have been involved in creating five new companies in Florida. These companies alone have brought $11.84 million in additional external funding and added at least 45 high-tech and high-paying jobs to the state.

Appendix C provides a list of additional funding reported by Program grantees in 2009.

"This program has really jump started my academic career as a new investigator and helped support a young and growing Division of Imaging Research in our department."

Kevin Johnson, 2008 NIR, University of Florida

Improving the Health of Florida's Citizens

The purpose of the Program's diverse investment in research is to bring improved health care and health to the people of Florida. Many Program grantees are far along in the process of bringing new diagnostics, treatments, and devices to patients. Twenty-three studies involving more than 2,000 human research subjects have helped to build a bridge between exciting research findings and clinical need. For example, some studies have looked at specific genetic markers in patients with lung cancer, with an eye toward improving diagnosis and treatment of this disease.

"…Through my grant travel allowance, I was able to attend the Society for Research on Nicotine and Tobacco annual meetings, where I started networking with other researchers. Slowly they began to realize that our animal model is scientifically a very strong model. In addition, they realized that the scientific possibilities and the use of this animal model in nicotine research are tremendous. Currently, I collaborate with a few well-known nicotine researchers, who are very supportive of my research and are willing to help me strengthen this line of research."

Susanne Cappendijk, 2006 NIR, Florida State University

Another study is researching the effectiveness of a program designed to reduce adult smoking rates by educating parents about the harmful effects of environmental tobacco smoke on children. Program grantees have filed twenty patents that involve a clinical improvement towards better prevention, diagnoses, treatments, and cures. These clinical studies are critical to translating scientific discoveries into products and programs that are essential for preventing and reducing the consequences of tobacco-related disease.

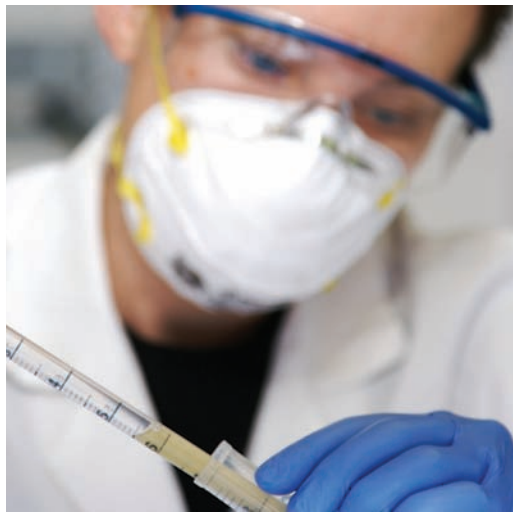
Investing for the Long-term

It may often take a decade or more to translate an exciting scientific insight into a new application for preventing, diagnosing, treating, or curing disease. The Program's focus on funding exploration of new scientific discoveries, sustaining research momentum, training physician-scientists, and facilitating commercial research collaborations is helping to make that journey from laboratory bench to a patient's bedside a successful one. Increasing the likelihood that funded projects reach their long-term patient goals enhances the state's ability to reap the long-term fiscal and health benefits of its investments in its biomedical research community and infrastructure.

2009 Accomplishments

In 2009, the Program funded 45 research projects totaling $20.5 million. Several of these grants support research into new biologic or genetic markers that can be used to predict risk, diagnose disease, and guide more effective treatments for tobacco-related illness. Other awards are for the evaluation of a variety of behavioral programs that may keep people from lighting that first cigarette or help those who want to quit smoking succeed in their endeavors. A number of grants are placing new investigators on track toward successful careers investigating novel ways to prevent, diagnose, and treat tobacco-related illness, while others will give established investigators additional support as they move promising projects - from laboratory studies in cells or animal models toward clinical human testing. Some grants are stimulating collaboration between Florida's academic centers and private industry, moving innovative product ideas toward commercial markets while providing additional opportunities for economic growth within the state. Additional information about this year's awards is in Table 3 and Table 5 in the "2009 Grant Awards" section.

The following pages describe the Program's decade of accomplishments in tobacco-use behavior, cardiovascular disease, cancer, stroke, and pulmonary disease. Included are highlights of funded research and profiles of a few of many grant recipients who are using the Program's dollars to improve Florida's physical and fiscal health today and for the future.



"I am a new investigator... The program gave me the opportunity to develop my own ideas as well as to collaborate with other scientists. We have generated data for eight publications and four provisional patents. This is a real opportunity for new scientists to contribute with new ideas and research work in translational and basic research directed to alleviate the human suffering induced by tobacco."

Valentina Echeverria-Moran, 2007 NIR
Bay Pines VA Healthcare System

Behavioral Research

Tobacco avoidance and cessation measures are key to reducing the 443,000 lives and more than $200 billion that are lost to cigarette smoking each year in the United States. Approximately 2,800 Americans become regular smokers every day, including 1,000 individuals under the age of 18. While it is easy to begin smoking, quitting is more difficult. This is because nicotine alters brain function and produces dependence. Studies show that nicotine is as addictive as heroin, cocaine, or alcohol. Individuals trying to quit smoking must overcome symptoms of nicotine withdrawal, such as irritability, anxiety, loss of concentration, and increased appetite.[2]

While counseling, medication, and education can help increase the success of cessation programs, many people trying to quit make multiple attempts and/or relapse during the process. As a result, although 70 percent of smokers want to quit completely and 40 percent try to quit each year, fewer than 10 percent succeed.[3] Gaining a better understanding of the environmental, psychological, and physiological factors that lead people to begin smoking and reducing obstacles to quitting are important for improving tobacco prevention and cessation strategies.

Reducing the number of smokers in Florida would provide important fiscal and health benefits to the state. A recent study suggests that every dollar invested in smoking cessation efforts will provide a nearly two- or three-fold economic gain for Florida.[4]

A Decade of Achievement

21 Total Behavioral Research Grants

131 Presentations

35 Publications

$9.1 million Total Behavioral Research Funding

$12.5 million Follow-on Research Funding

Beyond the Numbers: Behavioral Research in Action

The research of Dr. Carlos Bolaños, Florida State University 2007 New Investigator Research (NIR) grantee, is receiving national and international attention for a "groundbreaking study showing a link between teenage smoking and long-term depression that lasts into adulthood." [5]

"We published in Neuropsychopharmacology, and the Society for Neuroscience issued a press release on our findings." In addition, eight other scientific or health-related websites have picked up the story, National Public Radio interviewed Dr. Bolaños, and international radio stations want to report his findings. Dr. Bolaños' focus is nicotine exposure in adolescent animals, which is the stage of life when most people start smoking. To date, the vast majority of nicotine research has been in adults.

2009 Accomplishments

In 2009, the Program awarded three new NIR grants for behavioral research. One funded project is evaluating the relationship between nicotine and control of attention deficits. Another seeks to reduce children's exposure to secondhand smoke by developing a program that helps parents reduce their smoking habits. The third is studying the effects of secondhand smoke on depression in women who are pregnant or have recently given birth.

A New Beginning in Tobacco-Related Research

Mary Gerend, Ph.D.
Florida State University

2007 New Investigator Research Grant

As an undergraduate, Dr. Gerend was involved in tobacco-related behavioral research and took a great interest in the field. During her graduate school studies, she stepped away from tobacco-related research, focusing instead on women's health issues. Now, as a young investigator in the Department of Medical Humanities and Social Sciences, Dr. Gerend is using her funding from the Program to return to tobacco-related behavioral research while she also pursues her interest in women's health. In 2007, the Program awarded Dr. Gerend a $375,000 grant in support of her efforts to develop a smoking cessation program tailored to the needs of smokers with anxiety sensitivity. These individuals, who have a high risk for anxiety disorders, may have particular difficulty quitting smoking because the side effects of nicotine withdrawal mimic their anxiety-related sensations. With this grant, the Program is helping Dr. Gerend make an impact in the lives of some Florida smokers.

Meeting the Needs of Patients who Want to Quit Smoking

"Individuals with anxiety sensitivity have unique needs and challenges when they try to quit smoking," explained Dr. Gerend. "With the grant from the Program, we've developed a 12-week behavioral program designed to meet those needs. The program helps these individuals become more comfortable with anxiety-related sensations in a safe and controlled environment. After nine weeks of learning to manage these sensations, they attempt to quit smoking, supported by three additional weeks of group counseling and support. Our early results look promising, and I am very excited that our work is making an immediate difference in Floridians' lives." Dr. Gerend's behavioral therapy program utilizes nicotine patches, but does not include other medication. This may make the program more accessible to individuals concerned with the potential side effects of medical therapies.

Building Florida's Biomedical Research Community One Investigator at a Time

Dr. Gerend exemplifies the Program's vision for bringing passionate researchers and cutting-edge science to Florida's tobacco-related research community. Although funding for behavioral science is difficult to obtain from federal sources such as the NIH and National Science Foundation (NSF), it is a core component of the Program's mission. "I've been interested in tobacco-related behavioral issues for many years, and my grant from the Program has allowed me to return to one of my passions and start a career in this area," she said. "In addition to the financial funding, my award from the Program has created additional opportunities for me to observe and participate in cutting-edge behavioral research strategies, which will be critical to my long-term productivity in this area. Dr. N. Brad Schmidt, my mentor, and Dr. Natalie Sachs-Ericsson, my co-investigator, provide me with invaluable scientific insight and helpful advice on being an effective project leader, administrator, and grant applicant."

Dr. Gerend credits her Program grant with helping her secure funding from the National Cancer Institute (NCI) to support one of her women's health projects. "I believe that having a peer-reviewed grant on my application, and a track record of successful grant administration, gave the NCI confidence in my scientific and administrative capabilities," added Dr. Gerend.

Now in data-collection mode, Dr. Gerend expects that she will soon have the information she needs to develop a manuscript for publication and apply for additional external funding to support her tobacco-related behavioral research. The data generated with the Program's support should help to make her more competitive in securing federal funding in this area. In the meantime, her ongoing study is helping more Floridians kick the cigarette habit, which is a long-term goal of the Program.

Cardiovascular Disease

Smoking is one of six major risk factors for cardiovascular disease (CVD) and is the greatest risk factor for coronary heart disease in people under the age of 50. Smoking leads to the buildup of fatty deposits in the arteries, which is a major cause of coronary heart disease. Smokers also have an increased risk for high blood pressure.[6] Data from 2005 indicate that heart disease causes between 650,000 and 860,000 deaths annually. A recent report from the American Heart Association estimates that health care services, medications, and lost productivity associated with heart disease will cost more than $300 billion in 2009 alone.[7]

Heart disease also is the leading cause of death in Florida. More than 54,000 people in Florida died of CVD in 2007, the most recent year for which data are available.[8] It is estimated that the annual direct costs of high blood pressure and heart disease in Florida were $2.4 billion and $4.5 billion, respectively. The true costs of these diseases within the state are even higher when indirect costs, such as lost productivity, are included.[9]

A Decade of Achievement

40 Total Cardiovascular Disease Grants

145 Presentations

56 Publications

$17.8 million Total Cardiovascular Disease Funding

3 Patents

$27.4 million Follow-on Research Funding

Beyond the Numbers: Taking on the #1 Cause of Death in the United States

Everyone knows exercise is good for your heart. But Dr. Scott Powers, 2001 Investigator-Initiated Research grantee at University of Florida, figured out one reason why. He used his King grant to identify an antioxidant enzyme that is produced through exercise and which protects the heart against heart attack. He leveraged his Program funding to earn $2 million from the NIH and the American Heart Association. Dr. Powers explained that this funding in turn generated more research and "at least three or four drug development companies are interested in drug discovery based on this finding. It has a lot of potential for cardio protection and could protect organs during transplant as well. In addition to this advancement, my additional funding also allowed me to train seven people-students and technicians-in my lab and brought dollars to the University. I'm very grateful for the King funding. Without it, I wouldn't have had the resources to get preliminary data, and I don't believe I would have gotten federal funding or launched a research enterprise."

2009 Accomplishments

The Program awarded nine CVD-related grants in 2009. The combined value of these grants is $3.5 million. Research projects supported by these grants will evaluate the relationship between heart disease and certain types of hypertension; mechanisms that regulate the formation of new blood vessels; the role of inflammation in narrowing of blood vessels; and the impact of nicotine on the accumulation of fatty deposits within the blood vessels and subsequent coronary heart disease. Each of these projects seeks to advance the understanding of how CVD develops and progresses.

Investing in Florida's Biomedical Future Attracts Dedicated Researchers Today

Currently an investigator at the Burnham Institute, Dr. Layton Smith received his award when he was an investigator at Scripps Florida. When he moved between institutions, he was able to transfer his Program grant and continue his research. Dr. Smith used his award from the Program to help launch his independent research career, which is focused on the study of biologic pathways that regulate blood pressure. Smokers are at increased risk of developing high blood pressure, and Dr. Smith's work seeks to provide new targets for therapy.

Dr. Smith's experience as a young investigator embarking on an independent research career in Florida is a powerful example of the importance of investing in the state's biomedical research infrastructure and grant programs. It also highlights the role that the Program plays in the state's overall portfolio of biomedical research investments.

After completing his post-doctoral fellowship, Dr. Smith evaluated a number of promising job opportunities. "Naturally, I looked at positions in the established biomedical research centers in the northeast and the mid-Atlantic corridor," he explained. "But then I looked at Florida – the state in which I had grown up – and saw that the state had made tremendous investments in building biomedical research infrastructure. Recruiting leading research organizations such as The Scripps Research Institute, Burnham Institute for Medical Research, and the Torrey Pines Institute for Molecular Studies has really put Florida on the map as a center for leading-edge biomedical research. I realized that Florida would give me the scientific environment I needed to do the kind of science for which I had trained so long to do. Even better, it allowed me to return to the strong family roots I already had in the state."

A Warm Welcome for a New Investigator

Upon his arrival in Florida, Dr. Smith discovered that the state also had much to offer in terms of financial support for young investigators. "A few weeks after joining The Scripps Institute, I learned of the James & Esther King Program and the grants it provides to new investigators," he said. "I saw this as a tremendous opportunity to secure funding for my research at a time when the NIH budget was flat and federal funding for basic science was very difficult to get. Funding limitations make the transition to an independent researcher very challenging. The three-year, $427,500 award I received from the Program provided the foundation on which I've launched my career."

An Investment That Pays Off

Within a year of receiving the award from the Program, Dr. Smith had generated sufficient data to obtain a $216,375 grant from the NIH. The results of his research are being considered for publication, and he submitted an application for a $1.25 million NIH grant in October 2009 to extend the research started with funds from the Program.

"The Program is a critical component of the state's biomedical research investment strategy," added Dr. Smith. "The best way to leverage Florida's investment in infrastructure is to support researchers. The Program effectively fulfills the unmet funding needs of new investigators. The success I've achieved as an independent investigator is entirely based on work funded by the Program. Without it, I wouldn't be here."

Layton Smith, Ph.D.
Burnham Institute

2006 New Investigator Research Grant

Cancer

According to the National Cancer Institute, cigarette smoking causes 87 percent of deaths from lung cancers, the leading cause of cancer death in the United States. Cigarette smoking also increases the risk of other cancers, including throat, mouth, pancreas, kidney, bladder, and cervical cancer.[10] Lung cancer is the second leading cause of death in Florida.[11] In 2007, the most recent year for which data are available, cancer of the trachea, bronchus, and lung caused 11,650 deaths in the state, and 4,730 Florida residents died from cancers of the mouth, throat, pancreas, bladder, and cervix. These cancers cause tremendous loss of life and also impose a significant financial burden on patients' families and the state.

A Decade of Achievement

32 Total Cancer Grants

260 Presentations

118 Publications

$20.3 million Total Cancer Funding

$18.7 million Follow-on Research Funding

Beyond the Numbers: Innovative New Cancer Therapies

When Dr. Thomas Shellenberger, M.D. Anderson 2008 NIR grantee, came from Texas three years ago, "the research program at our center was only an idea," he described. "The James & Esther King and Bankhead-Coley grants are the first grants we have had. They have provided a basis on which we have built our research program in Orlando. They have had a huge impact in getting our program off the ground and in getting our research up and running, which is challenging enough for a physician scientist in an established academic center. We've found an important pathway in which head and neck cancer spreads through a phenomenon called "perineural invasion"— in which cancer cells attack nerve trunks in the local area and spread centrally. There is little known about the phenomenon at the basic level while the clinical impact for head and neck and other cancers is legion. Therefore, bringing a clinical background is critical to the investigation to develop targeted therapies."

Dr. Shellenberger launched his research program while training a research fellow, Dr. Rafael Madero, a physician who joined M.D. Anderson in 2006. The team's research findings have been presented at the annual meetings of the American Head and Neck Society, the American Association of Cancer Research, and the American Society of Clinical Oncology.

Dr. William Self, University of Central Florida, 2005 NIR grantee, described the impact of his grant. "The King grant was critical for me and was one of my first funded proposals. Using this funding, I was able to recruit students, get my lab going, and build a good reputation in the field through strong publications and attending national meetings. This led to further funding from both NIH and NSF, and now I currently have several federally funded grants. Without this initial funding I believe it would have been more difficult to get things moving at an early stage in my career."

2009 Accomplishments

In 2009, the Program awarded 15 grants in the area of cancer research: one Bridge Grant, five RC1 (Florida Research Challenge) Grants, one TSP (Team Science Program) Grant, two Technology Transfer/Commercialization Partnership (TTCP) Grants, and six NIR (New Investigator Research) Grants. These grants support diverse projects, including the following:

- Research into improved methods for predicting which cancer therapies will work best
- The biology and genetics of cancer
- The impact of genetic and environmental factors on lung cancer survival
- Novel cancer therapies and mechanisms of resistance to current therapies

Each of these research areas holds enormous potential for advancing the treatment of cancer and improving clinical outcomes for cancer patients in Florida and around the world.

A Promising Start in a Critical Research Area

Karoline Briegel, Ph.D.
University of Miami

2005 New Investigator Research Grant

Dr. Karoline Briegel's award from the Program provided critical financial support as she embarked on independent breast cancer research, a disease with substantial unmet medical need. "At the time I applied to the Program, I had just been appointed Assistant Professor at the University of Miami," said Dr. Briegel. "I had not yet generated the data needed to apply for funding from the NIH or other federal agencies. My award from the Program allowed me to get started on an exciting research project that has resulted in a U.S. patent and spawned additional studies in other tobacco-related cancers."

The Program also provided Dr. Briegel with support from more experienced researchers. "My mentor gave me important insight into the clinical implications of my research. Now I am more focused on how my work can help cancer patients. Additionally, the constructive feedback I received as part of the Program's annual review process helped ensure the success of my research."

Dr. Briegel's successes include a patent application, two papers submitted for publication in peer-reviewed journals, and a one-year Braman Development Grant from the Sylvester Comprehensive Cancer Center. The data generated with her award from the Program has enabled her to submit a larger grant application to the NIH. However, she views the opportunity to help patients as her greatest success.

"My work has diagnostic and therapeutic potential in a type of breast cancer that is very difficult to treat. These patients don't respond well to current therapies and need new treatment options. Some of our studies suggest that the discovery may also have utility in treating metastatic breast cancer, as well as other tobacco-related cancers."

One Grant, Many Benefits

In funding Dr. Briegel, the Program has achieved several of its goals. Fostering a vibrant community of researchers in Florida focused on tobacco-related disease is one of the Program's key objectives, and Dr. Briegel is an example of the Program's mission in action. In training and employing two graduate students, a post-doctoral fellow, and a laboratory technician, she is further strengthening that community. Additionally, her work has provided new insight into the genesis and progression of cancer and opened the door to new diagnostics and therapies with the potential to improve the health of Florida's citizens, another Program objective. Licensing of her patent, which was presented at a gathering of pharmaceutical companies in October, could generate revenue for the University of Miami, which would help the Program achieve its goals of stimulating economic activity in the state and increasing Florida's per capita research funding.

Dr. Briegel's experience also demonstrates the value in the Program's philosophy of funding diverse basic research projects. "The Program is important because it provides seed funding for basic research projects that don't yet qualify for NIH funding," she explained. "It's by serendipity that my discovery has diagnostic and therapeutic potential in breast and other tobacco-related cancers. I didn't know at the start where this work would take me, but I am very excited about where it is going."

Stroke

Cigarette smoking is the number one preventable risk factor for stroke and has several stroke-related effects on the human body.[12] Cigarette smoke causes fatty deposits to accumulate in arteries, including the carotid arteries, which supply blood to the brain. Most strokes in the United States result from blockage of the carotid arteries. Other components of cigarette smoke contribute to stroke risk by increasing blood pressure, decreasing the oxygen content of blood, and making it easier for blood to form clots.[13]

Stroke is the third leading cause of death in the United States, killing more than 143,000 people each year. Stroke-related medical and disability costs in the United States are expected to reach almost $69 billion in 2009.[14] It is also the third leading cause of death in Florida. In 2007, the most recent year for which data are available, 8,715 deaths in the state were due to this disease.[15]

A Decade of Achievement

17 Total Stroke Grants

45 Presentations

24 Publications

$5.4 million Total Stroke Funding

$8.2 million Follow-on Research Funding

Beyond the Numbers: Preventing and Reducing a Dangerous Medical Condition

According to Dr. Bingren Hu, University of Miami 2007 Bridge grantee, tobacco use increases stroke severity and the incidence of stroke death by two- to three-fold. "The King grant has helped us to analyze the changes in the brain due to stroke injury. We now better understand the biochemical process that leads to protein damage. This understanding can help us learn how to prevent such damage and can lead to a cure." Dr. Hu explained his federal grant application would have been funded in more stable economic times, but his King grant is helping him prepare an even more competitive application for the next funding round.

2009 Accomplishments

In 2009, the Program awarded two NIR Grants, one TSP Grant, and two RC1 Grants in the area of stroke-related research, totaling $3 million. One of the NIR grants is funding a study focused on developing post-stroke rehabilitation programs that can restore function to the arms of stroke patients. The other NIR grant supports research into the impact of specific genetic variations on susceptibility to stroke. The TSP grant is focused on developing new drugs that can improve the safety and efficacy of stroke therapy. One RC1 grant seeks to reverse damage to injured nerve cells while the other is exploring a new multi-drug combination therapy for stroke.

Supporting New Ideas from an Established Investigator

For 40 years, Dr. Wu has focused his research on pathways within the brain that play important roles in health and disease. In 2007, the Program awarded Dr. Wu a one-year, $184,280 Bridge Grant to support ongoing research into the impact of smoke on a brain enzyme that helps control communication between brain cells. This enzyme also is involved in regulating the level of a molecule that is believed to cause death and damage to brain cells during stroke. Smokers are at a higher risk of stroke, and Dr. Wu is evaluating how smoke impacts this enzyme system. "I believe that research into this enzyme pathway may pave the way for novel approaches for preventing and treating stroke," said Dr. Wu. "It also may enable new tests for assessing alterations in the enzyme in individual smokers, providing them with a more personalized profile of their stroke risk and allowing earlier interventions to prevent stroke. We also want to evaluate if targeting this enzyme creates new ways to protect brain cells and limit damage in patients who experience a stroke."

The Program's Bridge Grant helped Dr. Wu continue this exciting research during a time when federal opportunities were contracting. "For many years, my stroke-related research was funded by grants from the NIH and NSF," explained Dr. Wu. "However, as federal research budgets contracted, my NSF grant was not funded, even though it had received a good priority score. My Bridge Grant from the Program allowed me to continue this project, and I was able to generate data that could support additional grant applications to federal agencies."

Building Capacity at an Expanding Florida Research Institution

Beyond supporting Dr. Wu's work, the Program has been instrumental in helping him build capacity in tobacco-related brain research at Florida Atlantic University (FAU). In 2005, the Program awarded a three-year, $450,000 NIR Grant to a young faculty member that Dr. Wu was mentoring. This grant subsequently led to a three-year, $820,800 TSP Grant awarded in 2008 by the Program to study how immune cells in the brain responded to nicotine and stress. Helping FAU build a critical mass in tobacco-related brain disease is consistent with the Program's philosophy of supporting biomedical research at institutions throughout Florida.

"Funding basic and applied science is one of the best long-term investments that Florida can make," said Dr. Wu. "Earlier in my career I worked at UCSF [University of California at San Francisco] and City of Hope in California. Research conducted at those institutions gave rise to novel therapies and was critical for establishing leading biotechnology companies. This has created jobs, expanded the tax base within the state, and provided hundreds of millions of dollars in licensing and royalty fees to those institutions. I believe that the James & Esther King Program could help Florida achieve similar success. Over the long term, that would benefit patients, as well as the state's biomedical research community, and overall economy."

Jang Yen Wu, Ph.D.
Florida Atlantic University

2007 Bridge Grant

Pulmonary Disease

Smoking causes a variety of pulmonary diseases, including chronic obstructive pulmonary diseases (COPD, also known as chronic lower respiratory disease, or CLRD) such as chronic bronchitis and emphysema, as well as pneumonia and lung cancer. Smoking also exacerbates asthma, and secondhand smoke leads to more than 200,000 asthma episodes nationwide each year. Among U.S. smokers, 73 percent of smoking-related conditions are chronic lung diseases.[16]

In Florida, COPD is the fourth leading cause of death. In 2007, the most recent year for which data are available, COPD caused 9,317 deaths in the state. A 2002 report by the Florida Department of Health showed that COPD was the only disease for which mortality rates had continuously increased in the state since 1950, with a four-fold increase between 1950 and 2000. Florida patients with COPD spent a combined total of 329,000 days in the hospital due to their disease in 2002, at a cost of $1.1 billion.[17]

A Decade of Achievement

43 Total Pulmonary Disease Grants

246 Presentations

99 Publications

$16.4 million Total Pulmonary Disease Funding

1 Patent

$55 million Follow-on Research Funding

Beyond the Numbers: Breathing New Ideas into Pulmonary Disease Research

Dr. Veena Antony, University of Florida (UF) 2004 TSP grantee, described how her King grant changed the course of pulmonary research at UF. "The King grant allowed us to open a Center for Excellence in Chronic Obstructive Pulmonary Disease. We leveraged King funds into NIH funding and dollars from private foundations. The University saw our ability to obtain funds and committed time, space, and dollars to establish the Center. Through this grant, we retained two faculty members and developed collaborations in multiple places throughout Florida. For patients, we better understand why smokers have a propensity to develop infection and why lung function continues to drop even after smokers quit. The King grant ignited the work, and it's just never stopped growing." After her grant completion, Dr. Antony became a member of the Program's Biomedical Research Advisory Council.

2009 Accomplishments

In 2009, the Program funded seven grants for pulmonary disease research with a total of $3.5 million. These awards will support research in pulmonary arterial hypertension, asthma, and COPD. Two of the awards are NIR Grants, providing important funding to help researchers embarking on independent research careers in pulmonary disease and the effects of tobacco. Another award is a TTCP Grant that has the potential to stimulate economic activity in Florida through the establishment of a new pharmaceutical company that is partnering with an academic researcher to develop new pulmonary disease therapies. These grants support research designed to provide new insight into the mechanisms of and potential treatment strategies for a variety of pulmonary diseases.

Generating New Insights into the Asthma Disease Process

Eckhard Podack, M.D., Ph.D.
University of Miami

2009 Technology Transfer/ Commercialization Partnership Grant

Dr. Eckhard Podack is using his award from the Program to support translational research that may lead to a new treatment for asthma. Translational research is the process of adapting and applying laboratory discoveries for use in the clinic. A growing body of data indicates that individuals with asthma are sensitive to smoking and that smoke enhances susceptibility to asthma attacks. Children in families with smokers have a higher risk and incidence of developing asthma.

Previously, Dr. Podack discovered that inhibiting the interaction between a particular protein (TL1A) and its receptor (TNFR25) on the surface of cells blocks a chain reaction that results in lung inflammation. As Dr. Podack explained, this is an exciting observation because, "the results of our studies in mice suggest that blocking this interaction in humans could provide a new approach to therapy, or possibly even a cure for asthma."

Translating Knowledge into New Therapeutic Approaches

Dr. Podack's initial studies were conducted using a mouse antibody against the TL1A protein. However, mouse antibodies cannot be used in humans because they stimulate an immune response that clears the antibody from the body. "My grant from the James & Esther King Program is funding our efforts to modify the antibody so that it looks more like a human protein. Such 'humanization' is necessary to ensure that the antibody will not induce an immune response that reduces its therapeutic effect. This is a critical step in advancing a potentially novel therapy that could hold great promise for asthma patients."

Under Dr. Podack's TTCP grant, he is humanizing the TL1A antibody in collaboration with a Florida-based drug development company, Heat Biologics. If these translational studies are successful, the company will advance the antibody to human clinical studies in patients with asthma.

"Although the NIH has recently increased its funding for translational research, this is a very competitive area of study and it can be more challenging to fund the translational studies than it is to fund the initial research," said Dr. Podack. "However, translational studies are essential for turning new discoveries into novel therapies. In my experience, a variety of other granting organizations will not typically fund this type of work. By providing TTCP grants, the Program is helping to advance ideas with great therapeutic potential to the next stage of development."

Creating Economic Opportunities from Scientific Innovation

In addition to supporting the advance of new therapies with the potential to improve the health of Florida's citizens, the Program's award to Dr. Podack also is contributing to the health of Florida's biomedical industry. By funding collaborations between academic and corporate researchers within the state, the Program's TTCP grants also support small, innovative companies that can provide an engine for the state's economic growth.

"Developing new biologic agents, such as the antibody against TL1A, requires substantial investments of time and money," Dr. Podack said. "Heat Biologics will need money from the private sector to support its drug development programs. The peer-review process associated with the grant I received from the Program has helped to validate the TL1A antibody project in the eyes of investors. There are several venture capital funds now looking at investing in the company. If the company can raise money that allows it to expand its operations, that would bring additional jobs to the state."

Program Recognition and Evaluation

Reviews of the Program have occurred at both the national and state level. At the Program's request, the NCI evaluated the Program's peer review and funding decision processes in 2007. In 2009, the Florida Senate conducted a legislatively mandated review, and the Department of Health began an internal evaluation as well.

Programs Manager Sherrie Hajek accepting James & Esther King Program award from Dan Berglund, State Science and Technology Institute President and CEO.

National Recognition

In October 2009, the King Program received a national award from the State Science and Technology Institute (SSTI) at its 13th annual conference. SSTI is a national nonprofit organization that leads, supports, and strengthens efforts to improve state and regional economies through science, technology, and innovation. Its annual conference attracts many of the top decision makers and practitioners from every critical element of the technology-based economic development community – state, regional, university, nonprofit, private industry, and federal.

SSTI bestowed six achievement awards for organizations demonstrating best practices in building technology-based economies. In the category of "Expanding the Research Infrastructure," the James & Esther King Program was named the winner.

"The King Program stands out because of the breadth of initiatives funded with state funds," said Dan Berglund, SSTI President and CEO. "The program's focused efforts to elevate Florida's biomedical research community have enabled new research faculty to jumpstart their careers and established researchers to continue their worthy efforts in investigating tobacco-related illnesses."

National Program Evaluation

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

In late 2007, the NCI added these two programs, under the umbrella of the Florida Biomedical Research Programs, to its list of only 17 funding programs in the country meeting its rigorous standards for peer review.[18] Of these 17 programs, only one other is a state-level program. This means that cancer centers in Florida can count research grants from the Bankhead-Coley and James & Esther King Programs toward their required research base in qualifying for and maintaining multi-million dollar NCI Cancer Center Support Grants (CCSG).

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

By earning this important NCI recognition, the James & Esther King Program is helping close this gap by providing all five of Florida's cancer centers with an important advantage in competing for and retaining NCI Cancer Center designation,[19] along with the accompanying multi-million dollar federal awards.

State Program Evaluation

In 2006, the Legislature authorized extended support for the Program and required a review of its performance, outcomes, and financial management during the 2010 Regular Session of the Legislature. This review is intended to inform the Legislature, as the statute establishing the Program expires January 1, 2011, unless reenacted before that date (See Appendix A).

External Program Evaluation

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

The Recommendations section of the report contains the following statements:

> *Senate professional staff recommends that the Legislature re-enact the King Program and the Bankhead-Coley Program. These programs are achieving the goals established in statute and are benefiting the state in a variety of tangible and intangible ways. . . . The King Program is leveraging research funding in the state for improvement of tobacco-related health conditions, expanding the foundation of biomedical knowledge, improving the quality of the state's academic health centers, increasing the state's per capita funding for research, and stimulating the economy."*
>
> *The 2009 Legislature identified a recurring source of funding for these two programs that will provide stability and solidify the state's commitment to invest in biomedical research. This will enhance Florida's competitive position for external funding opportunities and attracting additional biomedical and biotechnology industry to the state.*

Internal Program Evaluation

In 2008, the Department began a comprehensive internal program evaluation of the James & Esther King Biomedical Research Program. The evaluation took a multi-faceted and long-term approach including:

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

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

Planning for the Future

The recent increase in state funding is an important endorsement of the James & Esther King Program's ability to identify and capitalize on strategic opportunities to enhance Florida's tobacco-related research capabilities.

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

The Program began the planning process in September by conducting three 90-minute conference calls for Program staff, the Advisory Council, invited speakers, and interested members of the public and culminated with a two-day planning retreat in November. Topics for the conference calls included:

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

With the benefit of this background work, the planning effort continued in a two-day working session in Orlando in mid-November. During this meeting, the Advisory Council analyzed the Program's research portfolio and progress toward its statutory goals, weighed opportunities for improving impact, and began setting a course for future funding strategies and priorities. As this report goes to press, the results of this planning effort are being compiled into a document that the Advisory Council expects to ratify at its January 2010 meeting.

Recommendations for Policy Change

According to (s.) 215.5602, *Florida Statute (F.S.)*, the Program is scheduled to expire January 1, 2011, unless reenacted by the Legislature before that date. The 2010 Legislature will determine the most appropriate funding source and means of funding these programs.

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

2009 Grant Awards

Planning for the 2009-2010 awards began with the assumption that the funding cycle would be similar to the previous year, and the Program planned to award approximately $8.4 million based on funds available. However, the Program experienced a number of changes in funding levels this year, impacting the grant award cycle. Early in the year, Florida's budget challenges created decreases in funding levels, and the Program experienced a 25 percent budget reduction. However, Florida lawmakers approved a cigarette surcharge and decided to use some of the revenue to increase appropriation to the Program, boosting Program funding for fiscal year (FY) 2009-2010. The Program took quick action to put the increased appropriation to work. The Advisory Council recommended $10 million in funding for projects for the FY 2009-2010, while at the same time electing not to lower Program standards for scientific merit by selecting more proposals for funding from the existing pool of applications. Instead, the Council recommended a second competition, the "2009-2010 Special Calls for Applications" (Special Calls), offering different grant mechanisms/types designed to meet additional Florida tobacco-related research needs.

Table 2 - Grant Mechanisms Offered in Regular Annual Call

Grant Mechanism	Purpose	Maximum Amount & Duration
Bridge Grant	To provide interim support for promising cancer research projects that have been highly rated by national panels of scientific peer reviewers in recent federal competitions but were not funded due to budgetary constraints. Researchers use the Bridge grant to collect preliminary data and improve their national applications based on peer review feedback.	$200,000 for one year
New Investigator Research (NIR) Grant	To foster development of new investigators so they can undertake independent research that will be competitive for national research funding. New investigators are those who have been full-time faculty for less than six years and have not received a large ($100,000 or more) peer-reviewed national grant. A senior researcher serves as a mentor.	$375,000 over three years
Team Science Program (TSP) Grant	To provide support for broad-based, multidisciplinary research programs with well-defined major objectives. TSP grants consist of at least three, but no more than five, interrelated yet individual research projects directed toward well-defined research goals.	$1,000,000 over two-three years
Technology Transfer/ Commercialization Partnership (TTCP) Grant	To encourage the collaboration of investigators at Florida research institutions and small biomedical businesses; stimulate technology transfer activities for promising research discoveries; and strengthen a project's economic feasibility and commercialization prospects.	$100,000 for one year

Results of the FY 2009-2010 Annual Calls for Grant Applications

The Program released the "Calls for Grant Applications: Medical, Biological, Behavioral, and Social Scientific Research and Development Fiscal Year 2009-2010," (the Calls) on December 1, 2008. (A Call is the published document announcing requests for grant applications.) Four grant mechanisms began on July 1, 2009: Bridge Grants, New Investigator Research Grants, Team Science Program Grants , and Technology Transfer/Commercialization Partnership Grants. Table 2 provides a brief description of each mechanism.

The Program completed the application review and award process in June 2009, and the Advisory Council recommended funding 25 grants totaling over $10 million, with projects beginning July 1, 2009. This action resulted in an overall proposal-to-award ratio of 43 percent. Table 3 provides a breakdown of requests and awards across the grant mechanisms.

Table 3 – 2009-2010 Grant Applications Received/Awarded

Grant Mechanism	Applications Received	Applications Awarded	Percent of Applications Awarded	Awarded Funding Amounts
Bridge Grant	6	3	50%	$ 451,184
New Investigator Research	41	18	44%	$ 6,710,317
Team Science Program	6	3	50%	$ 2,764,174
Technology Transfer/ Commercialization Partnership	5	1	20%	$ 100,000
Total	**58**	**25**	**43%**	**$ 10,025,675**

Public and private research institutes throughout Florida are benefiting from these awards. The Program awarded grants to seven Florida research institutions. All seven of these institutions are beneficiaries of funds to support one or more new investigators, illustrating the broad distribution of new talent establishing independent research careers across the state.

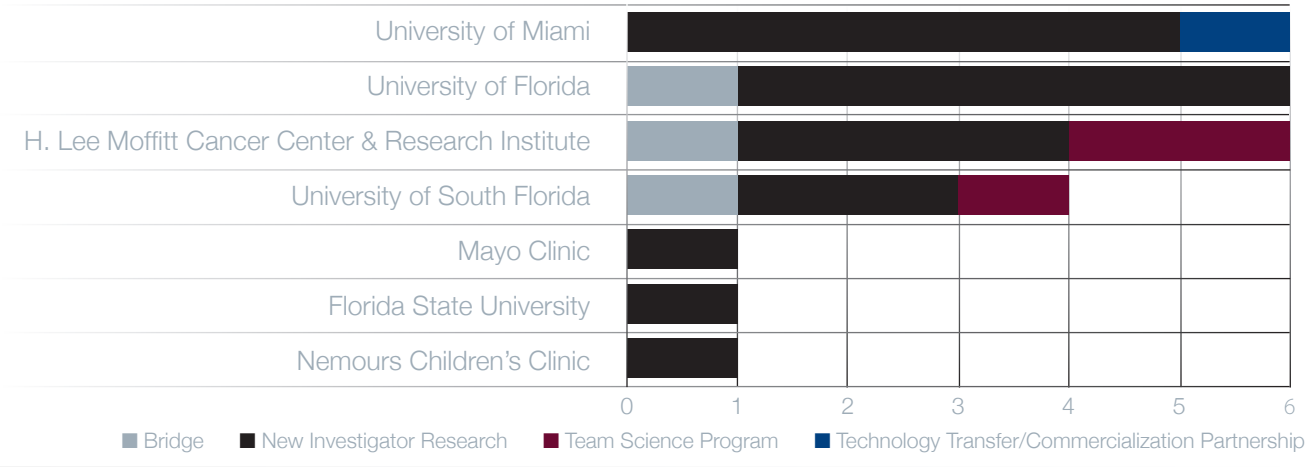


Figure 3 - Number of 2009-2010 Grants Awarded by Institution–Annual Call

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

Results for the 2009-2010 Special Calls for Grant Applications

In August, the Program released a second set of Calls for Grant Applications, offering grant mechanisms described in Table 4. One of the mechanisms, the TTCP grant, differed from the others in that it solicited applications any time between August 10, 2009 and January 29, 2010. The Program reserved up to $1 million for these awards. Measured against a pre-established merit score threshold, proposals were peer reviewed as received and either funded or declined within 60 days of application. The purpose of this flexible design was to be more responsive to commercialization opportunities involving small business and academic partnerships as they arose.

Table 4 - Grant Mechanisms Offered in Special Call

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

In this second competition round, 31 eligible applications were received. The Program completed the application review and award process in November 2009, and the Advisory Council recommended funding 20 research grants totaling $10.5 million, with projects beginning January 1, 2010. This action resulted in an overall proposal-to-award ratio of 65 percent. Table 5 provides a breakdown of requests and awards across the grant mechanisms.

Table 5 - 2009-2010 Grant Applications Received/Awarded in Special Calls

Grant Mechanism	Applications Received	Applications Awarded	Percent of Applications Awarded	Awarded Funding Amounts
Research Challenge Grant	19	11	58%	$ 7,685,214
Shared Instrument Grant	8	7	88%	$ 2,622,377
Technology Transfer/ Commercialization Partnership	4	2	50%	$ 199,999
Total	**31**	**20**	**65%**	**$ 10,507,590**

As illustrated in Figure 4, a number of public and private research institutes throughout Florida benefited from grants awarded. The Program awarded grants to five Florida research institutions as a result of the Special Calls.

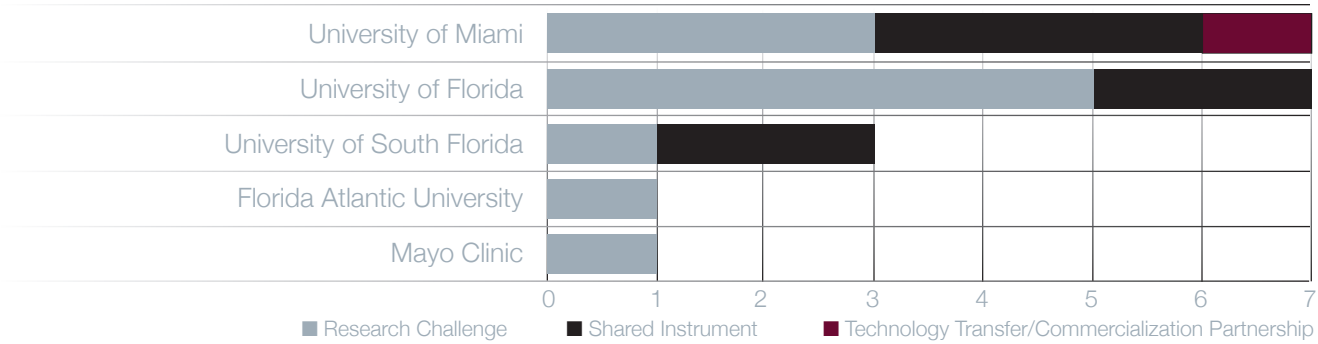
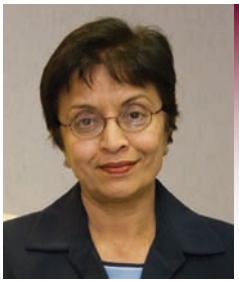


Figure 4 - Number of 2009-2010 Grants Awarded by Institution - Special Calls

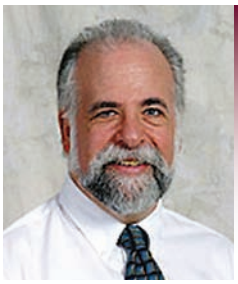
Biomedical Research Advisory Council

Section 215.5602, *F.S.*, charges the Program with awarding grants for tobacco-related research through the James & Esther King Biomedical 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 Bankhead-Coley Cancer Research Program.



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

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



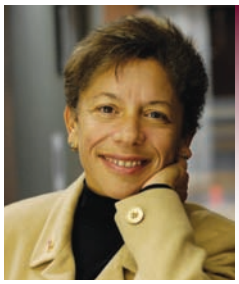
Richard J. Bookman, Ph.D.
Executive Dean for Research & Research Training and Vice Provost for Research
Miller School of Medicine
University of Miami
Seat: Advisory Council Chair and American Heart Association
Appointed: July 1, 2000

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

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

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

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



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

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

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

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

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

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

The 11 appointees to the Biomedical Research Advisory Council:

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

National Biomedical Research Funding and Funding Trends

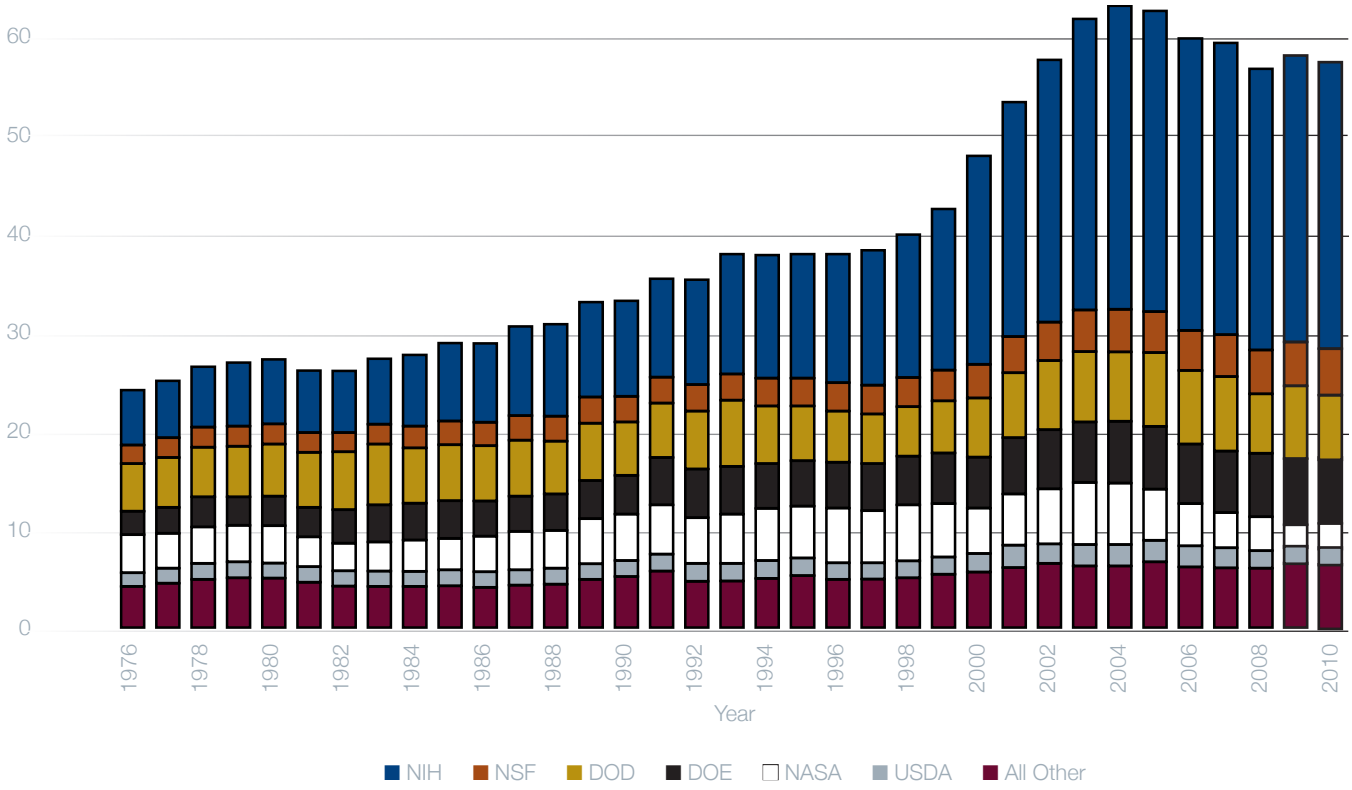
National biomedical research funding and funding trends provide context in which to assess Florida's biomedical research funding priorities. Trend information also provides insight into the challenges and opportunities that Florida faces as the state seeks to attract biomedical research and industry jobs, at a time when other states are making similar efforts to establish and build their biomedical research communities.

National biomedical research funding has varied over time. From 1976 to 1998, the combined budgets for federal research agencies remained relatively steady (see Figure 5). Between 1998 and 2003, however, a campaign to double the NIH budget noticeably increased total federal research spending and led to a rapid expansion of funding for biomedical research. In 2004, as domestic spending was curtailed in response to growing federal deficits, the NIH and other federal agencies experienced a slowing and then a contraction of their budgets.[20]

A recent analysis of the proposed Federal FY 2010 budget conducted by the American Association for the Advancement of Science (AAAS) indicates that the NIH budget for Federal FY 2010 will increase by $443 million (1.4 percent) compared with 2009. The portion of the NIH budget devoted to research and development (which comprises 97 percent of the total budget) is anticipated at $30.2 billion. In addition to its annual budget, the NIH also received $10.4 billion from the American Recovery and Reinvestment Act (ARRA), which is to be spent through Federal FY 2010. According to the AAAS analysis, growth of the NIH budget, excluding ARRA funding, has declined since 2004 when adjusted for inflation. While NIH funding in Federal FY 2010 also is expected to fall behind overall inflation (1.6 percent), it will fare even more poorly compared with the inflation rate of biomedical goods and services (3.3 percent). Moreover, the inflation rate for goods and services purchased by the NIH budget has outpaced overall inflation by nearly two percentage points annually.[21]

It is important to keep in mind that ARRA spending will transiently boost NIH funding about one third above its formal 2010 budget. If the post-2004 budget trend and the growth of biomedical inflation continue, the buying power of federal research dollars will decline in the years ahead. In this scenario, direct investment by the state of Florida will continue to play a critical role in maintaining the health of the state's biomedical research community and its related economy. Similarly, continued funding by the Program will remain essential if Florida is to retain and advance its leadership in tobacco-related disease research.

In Florida's FY 2008-2009, researchers at 48 Florida-based organizations classified as domestic higher education, research institutes, independent hospitals, and industry received new NIH awards totaling $352 million. Preliminary results show that over 1,000 researchers in the state have received $465 million through October of FY 2009. This places Florida 17th among the 50 states as a percent of total NIH funding – up from 21st over the last 10 years – and 42nd on a per capita basis. (See Appendix E for a table of NIH funding by state.)



Source: AAAS analyses of R&D in annual AAAS R&D reports. FY 2010 figures are latest AAAS estimates of FY 2010 repuest. Research includes basic research and applied research. 1976-1994 figures are NSF data on obligations in the Federal Funds survey. ©2009 AAAS

Figure 5 – Trends in Research Dollars by Federal Agency, in billions

Program Operations

Summary of Program Funding History

Funding for the Program in fiscal year (FY) 2009-2010 included $2.2 million in interest earned on the $150 million reserve within the Lawton Chiles Endowment Fund and potentially $25 million appropriated from tobacco surcharge revenues (annualized estimate based on revenue generated from July - September 2009).

As this report goes to press, there have been 188 grants awarded since Program inception, representing over $79.2 million in research funding. Nearly half of these grants were awarded in 2009 with increased funding from the tobacco surcharge. Depending on the actual surcharge proceeds the Program receives during FY 2009-2010, more grants may be awarded in 2010, before the end of the fiscal year.

Table 6 below outlines the current number of grant applications received and the number, type, and total value of grant awards since 2005.

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.

2009 Budget Events

A number of factors impacted the Program's budget this year, creating a number of long-term changes in Program funding. The events and results are summarized below.

Impacts of FY 2008-2009 Budget Reduction

As an outcome of the special legislative session to address the State's revenue shortfall, the Program's FY 2008-2009 budget was cut by $1.5 million in January 2009. In response, the Program first reduced administrative expenses by canceling all remaining grantee site visits for the year and scaling back on the number of peer reviews of Bridge Grant applications in the FY 2009-2010 regular competition. The Department negotiated a corresponding reduction in its contract with Lytmos Group, Inc., a partner in Program oversight and administration.

Then, to address the balance of the reduction, the Program reduced its commitment to FY 2008-2009 grants by up to 9.25 percent each.

Table 6 - Five Year Program Award History

	FY 2009-10		FY 2008-09		FY 2007-08		FY 2006-07		FY 2005-06	
Applications	89		65		55		51		44	
Awards	No.	Million	No.	Million	No.	Million	No.	Million	No.	Million
IRR	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Bridge	3	$ 0.45	3	0.58	8	1.58	n/a	n/a	n/a	n/a
NIR	18	$ 6.70	16	5.86	14	5.17	12	5.05	11	4.85
RC1	11	$ 7.70	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
SBTT/TTCP	3	$ 0.30	2	0.20	n/a	n/a	2	0.19	2	0.20
SIG	7	$ 2.60	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
TSP	3	$ 2.80	2	1.77	2	2.00	3	2.85	3	2.99
Total	**45**	**$20.55**	**23**	**$8.41**	**24**	**$8.75**	**17**	**$8.09**	**16**	**$8.04**

Note: Numbers are rounded.

Impacts of FY 2009-2010 Budget Increase

During the regular session in 2009, the Legislature replaced the Program's general revenue appropriation with an appropriation of 2.5 percent of the revenue generated from the cigarette surcharge enacted in 2009, not to exceed $25 million per year.

Prior to awarding the 25 new grants that began July 1, the Program elected to restore its original funding commitments to FY 2008-2009 multi-year grants whose budgets had been reduced. In addition, the Program resumed making grantee site visits and released a set of "Special Calls for Grant Applications" in August 2009, with 20 more awards announced in December. These research projects began January 1, 2010.

Program Management

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

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

Table 7 - Key Program Operation Activities

Program Area	Activities
Program Planning and Development	• Plan and implement Program logistics and funding cycles • Prepare and release the Call for Grant Applications • Develop and refine Program policies and procedures and Program materials
Application Processing	• Prepare for, accept, and process online applications and provide technical assistance • Complete an administrative review of applications, checking compliance with all requirements
Peer Review Management	• Develop evaluation materials • Recruit, assign, and manage reviewers for scientific reviews of applications and progress reports • Maintain confidentiality agreements and monitor reviewer conflicts of interest • Monitor 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)

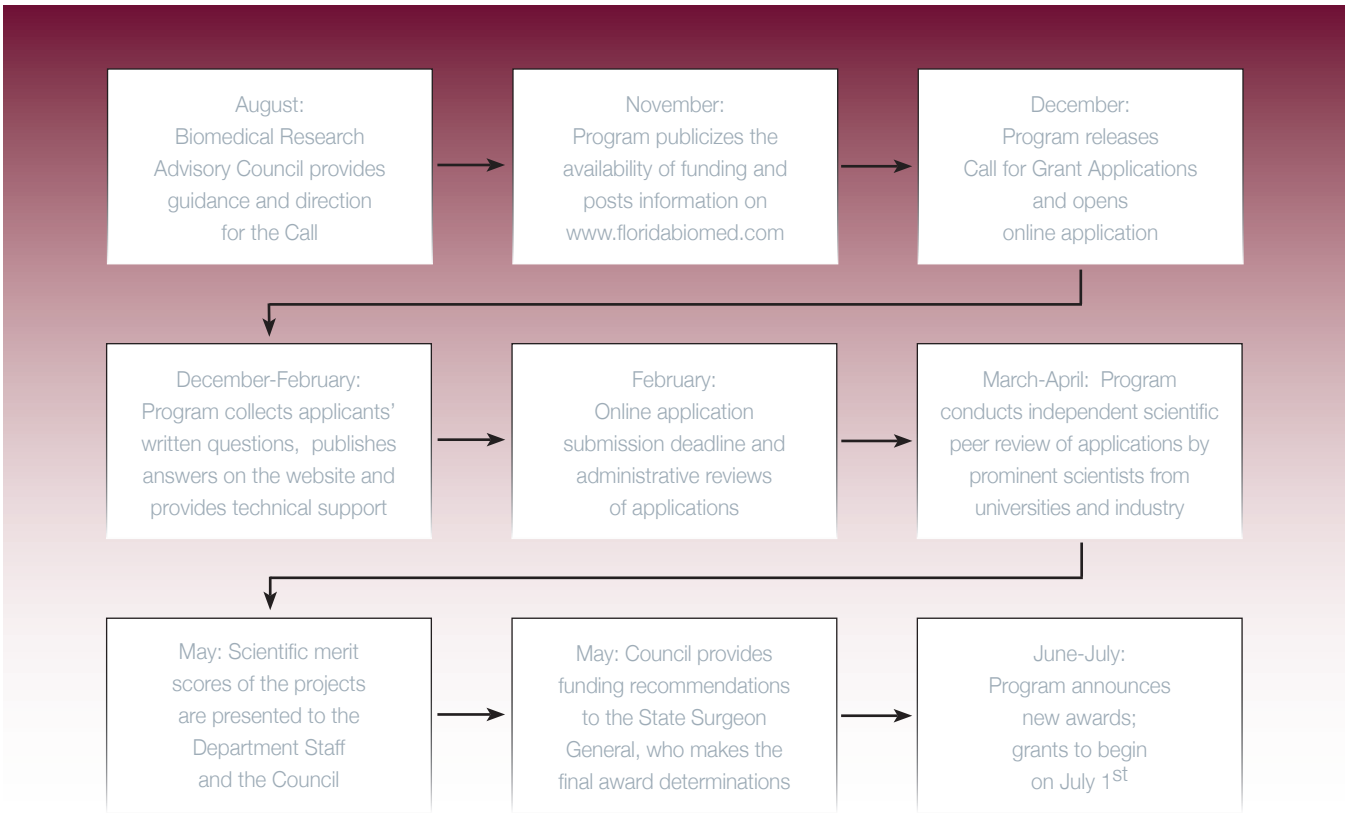


Figure 6 - The Annual Funding Cycle

How Grants are Awarded

The Program typically follows an annual cycle for soliciting applications and making awards, as illustrated in Figure 6 above. In evaluating proposals, the Program draws on the expertise of more than one hundred independent subject matter experts from outside Florida. These peer reviewers evaluate grant applications that match their specific expertise, rating scientific and technical merit and fit with programmatic goals. Unlike other peer review processes in which reviewers consult with each other, these reviews are performed independently and average scores compiled. To highlight the validity of this approach, the Program sought and received recognition from the NCI as having an approved peer review process.

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

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

How Grants Are Managed

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

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

Table 8 - Grant Management Processes and Tools

	Process or Tool	Value
Internal Controls	Signed terms and conditions (contract) with schedule of deliverables	• Defines expectations
	Grant Administration Manual	• Clarifies policies and procedures • Helps grantees comply with requirements
	Web-based system	• Provides grantees with convenient report submission • Serves as central data center • Provides efficient review of post-award deliverables
Financial Management	Regular review of budgets, financial reports, and expenditure changes	• Assures fiscal accountability
	Analysis of spending patterns	• Identifies potential accounting problems or project delays
Performance Management	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

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

Program Administrative Costs

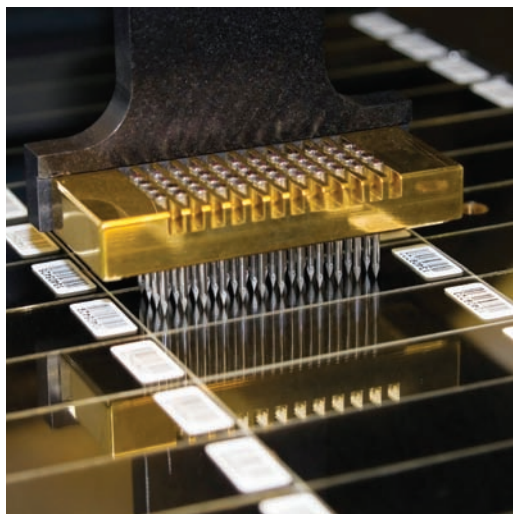
The Program by statute can use up to 15 percent of the appropriated funds for administrative expenses. As shown in Table 9 below, Program staff has held administrative costs below this legislative limit.

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

Table 9 - Program Expenditures (Millions)

Fiscal Year	Appropriation	Grant Expenses	Percent	Administrative Expenses	Percent
FY 09-10	24.98[a]	22.49	90%	1.79[b]	7%
FY 08-09[c]	8.40	7.32	87%	1.05[d]	13%
FY 08-09[e]	9.90	8.42	85%	1.25	13%
FY 07-08	9.90	8.75	88%	1.13	11%
FY 06-07	9.50	8.09	85%	0.88	9%
FY 05-06	9.37	8.04	86%	0.80	9%
FY 04-05	9.40	8.73	93%	0.68	7%
FY 01-04	17.64	16.45	93%	0.87	5%
Total (excluding FY 09-10)	**64.21**	**57.38**	**89%**	**5.41**	**8%**

[a] Annualized based on revenues collected for July, August, and September 2009.
[b] Projected expenses, includes $250,000 for the Center for Universal Research to Eradicate Disease pursuant to s. 215.5602(12), F.S.
[c] Mid-year revision due to budget reduction.
[d] Includes $68,703 for the Center for Universal Research to Eradicate Disease pursuant to s. 215.5602(12), F.S.
[e] Original grant awards and projected expenses prior to mid-year budget reduction.



Appendix A. Section 215.5602, *Florida Statutes* - James and Esther King Biomedical Research Program

(1) There is established within the Department of Health the James and Esther King Biomedical Research Program funded by the proceeds of the Lawton Chiles Endowment Fund pursuant to s. 215.5601. The purpose of the James and Esther King Biomedical Research Program is to provide an annual and perpetual source of funding in order to support research initiatives that address the health care problems of Floridians in the areas of tobacco-related cancer, cardiovascular disease, stroke, and pulmonary disease. The long-term goals of the program are to:
   (a) Improve the health of Floridians by researching better prevention, diagnoses, treatments, and cures for cancer, cardiovascular disease, stroke, and pulmonary disease.
   (b) Expand the foundation of biomedical knowledge relating to the prevention, diagnosis, treatment, and cure of diseases related to tobacco use, including cancer, cardiovascular disease, stroke, and pulmonary disease.
   (c) Improve the quality of the state's academic health centers by bringing the advances of biomedical research into the training of physicians and other health care providers.
   (d) Increase the state's per capita funding for research by undertaking new initiatives in public health and biomedical research that will attract additional funding from outside the state.
   (e) Stimulate economic activity in the state in areas related to biomedical research, such as the research and production of pharmaceuticals, biotechnology, and medical devices.

(2) Funds appropriated for the James and Esther King Biomedical Research Program shall be used exclusively for the award of grants and fellowships as established in this section; for research relating to the prevention, diagnosis, treatment, and cure of diseases related to tobacco use, including cancer, cardiovascular disease, stroke, and pulmonary disease; and for expenses incurred in the administration of this section. Priority shall be granted to research designed to prevent or cure disease.

(3) There is created within the Department of Health the Biomedical Research Advisory Council.
   (a) The council shall consist of 11 members, including: the chief executive officer of the Florida Division of the American Cancer Society, or a designee; the chief executive officer of the Florida/Puerto Rico Affiliate of the American Heart Association, or a designee; and the chief executive officer of the American Lung Association of Florida, or a designee. The remaining 8 members of the council shall be appointed as follows:
      1. The Governor shall appoint four members, two members with expertise in the field of biomedical research, one member from a research university in the state, and one member representing the general population of the state.
      2. The President of the Senate shall appoint two members, one member with expertise in the field of behavioral or social research and one representative from a cancer program approved by the American College of Surgeons.
      3. The Speaker of the House of Representatives shall appoint two members, one member from a professional medical organization and one representative from a cancer program approved by the American College of Surgeons.

      In making these appointments, the Governor, the President of the Senate, and the Speaker of the House of Representatives shall select primarily, but not exclusively, Floridians with biomedical and lay expertise in the general areas of cancer, cardiovascular disease, stroke, and pulmonary disease. The appointments shall be for a 3-year term and shall reflect the diversity of the state's population. An appointed member may not serve more than two consecutive terms.
   (b) The council shall adopt internal organizational procedures as necessary for its efficient organization.
   (c) The department shall provide such staff, information, and other assistance as is reasonably necessary to assist the council in carrying out its responsibilities.
   (d) Members of the council shall serve without compensation, but may receive reimbursement as provided in s. 112.061 for travel and other necessary expenses incurred in the performance of their official duties.

(4) The council shall advise the [1]State Surgeon General as to the direction and scope of the biomedical research program. The responsibilities of the council may include, but are not limited to:
   (a) Providing advice on program priorities and emphases.
   (b) Providing advice on the overall program budget.
   (c) Participating in periodic program evaluation.
   (d) Assisting in the development of guidelines to ensure fairness, neutrality, and adherence to the principles of merit and quality in the conduct of the program.
   (e) Assisting in the development of appropriate linkages to nonacademic entities, such as voluntary organizations, health care delivery institutions, industry, government agencies, and public officials.
   (f) Developing criteria and standards for the award of research grants.
   (g) Developing administrative procedures relating to solicitation, review, and award of research grants and fellowships, to ensure an impartial, high-quality peer review system.
   (h) Developing and supervising research peer review panels.
   (i) Reviewing reports of peer review panels and making recommendations for research grants and fellowships.
   (j) Developing and providing oversight regarding mechanisms for the dissemination of research results.

(5) (a) Applications for biomedical research funding under the program may be submitted from any university or established research institute in the

state. All qualified investigators in the state, regardless of institution affiliation, shall have equal access and opportunity to compete for the research funding.

(b) Grants and fellowships shall be awarded by the 1State Surgeon General, after consultation with the 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. Predoctoral and postdoctoral research fellowships.

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

(7) 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 conflict 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 shall be subject to the provisions of chapter 119, s. 286.011, and s. 24, Art. I of the State Constitution.

(8) The department may contract on a competitive-bid basis with an appropriate entity to administer the program. Administrative expenses may not exceed 15 percent of the total funds available to the program in any given year.

(9) The department, after consultation with the council, may adopt rules as necessary to implement this section.

(10) The council shall submit an annual progress report on the state of biomedical research in this state to the Florida Center for Universal Research to Eradicate Disease and to the Governor, the 1State Surgeon General, the President of the Senate, and the Speaker of the House of Representatives by February 1. The report must include:

(a) A list of research projects supported by grants or fellowships awarded under the program.
(b) A list of recipients of program grants or fellowships.
(c) A list of publications in peer reviewed journals involving research supported by grants or fellowships awarded under the program.
(d) The total amount of biomedical research funding currently flowing into the state.
(e) New grants for biomedical research which were funded based on research supported by grants or fellowships awarded under the program.
(f) Progress in the prevention, diagnosis, treatment, and cure of diseases related to tobacco use, including cancer, cardiovascular disease, stroke, and pulmonary disease.

(11) The council shall award grants for cancer research through the William G. "Bill" Bankhead, Jr., and David Coley Cancer Research Program created in s. 381.922.

(12) Beginning in fiscal year 2006-2007, the sum of $6 million is appropriated annually from recurring funds in the General Revenue Fund to the Biomedical Research Trust Fund within the Department of Health for purposes of the James and Esther King Biomedical Research Program pursuant to this section. From these funds up to $250,000 shall be available for the operating costs of the Florida Center for Universal Research to Eradicate Disease.

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

(14) The Legislature shall review the performance, the outcomes, and the financial management of the James and Esther King Biomedical Research Program during the 2010 Regular Session of the Legislature and shall determine the most appropriate funding source and means of funding the program based on its review.

(15) This section expires January 1, 2011, unless reviewed and reenacted by the Legislature before that date.

History.--s. 2, ch. 99-167; s. 4, ch. 2000-159; s. 2, ch. 2000-255; s. 5, ch. 2000-367; s. 4, ch. 2001-73; s. 1, ch. 2003-414; s. 8, ch. 2004-2; s. 3, ch. 2006-182.

[1]**Note**.—Chapter 2007-40 redesignated the Secretary of Health as the State Surgeon General.

Appendix B. Grantee Publications

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

Winter SL, Wong P, **Alexandrow MG**. In Vivo Chromatin Decondensation Assays: Molecular Genetic Analysis of Chromatin Unfolding Characteristics of Selected Proteins. *Methods Mol Biol*. 2009;523:27-40.

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Appendix C.
Related Awards Reported by Grantees

The following list represents $22.3 million in additional single and multi-year research awards reported since October 2008 by current and past grantees that are based directly on research findings from projects funded by the James & Esther King Biomedical Research Program. Grants are presented in alphabetic order by last name of the principal investigator, with the award year and grant type listed in parentheses.

Antony, V. (2004 TSP), "Second Hand Tobacco Smoke and Airway Infection." Flight Attendant Medical Research Institute, $375,000.

Barber, G. (2004 TSP), "Host Defense Regulation and Viral Oncogenesis." National Cancer Institute. $5,809,920.

Barber, G (2004 TSP), "Innate Intracellular Mechanisms." National Institute of Allergy & Infectious Disease. $252,250.

Barber, G. (2004 TSP), "Evaluation of Novel DExD/H Helicases in Innate Immune Signaling." National Institute of Allergy & Infectious Disease. $1,819,575.

Barber, G. (2004 TSP), "Targeted Therapy for Burkitt Lymphoma in Resource Poor Settings." National Cancer Institute. $496,972.

Barber, G (2004 TSP), "Mechanism of VSV-Mediated Oncolysis." National Cancer Institute. $299,221

Barber, G. (2004 TSP), "Host Defense and the Regulation of Interferon Production." National Institute of Allergy & Infectious Disease. $382,500.

Cappendijk, S. (2006 NIR), "The Identification, Localization and the Functionality of Nicotinic Acetylcholine Receptors in the Zebra Finch." National Institute on Drug Abuse, $212,537.

Chen, L. (2006 NIR), "Prostasin's Role in Epithelial Cell Shape Remodeling and Gene Expression Regulation." National Science Foundation, $600,000.

Copland, J. (2005 TSP), "TGF Beta Receptor Biology in Human Renal Cell Carcinoma." National Institutes of Health. $381,805.

Echeverria-Moran, V. (2007 NIR), "Molecular Mechanisms Underlying the Neuroprotective Actions of Cotinine." Alzheimer's Association, $100,000.

Echeverria-Moran, V. (2007 NIR), "Cotinine as a Therapeutic Agent Against AD." Johnnie B. Byrd Sr. Alzheimer's Center & Research Institute. $50,000.

Eichler, D. (2008 Bridge), "Regulation of the Endothelial Citrulline-Nitric Oxide Cycle." National Institutes of Health. $832,794.

Elliot, S. (2001 IIR), "Role of Notch Signaling in Endothelial Bone Marrow Stem Cell." National Institute on Aging. $340,425.

Fields, A. (2006 TSP), "PKC Iota Inhibition as a Therapeutic Strategy in Squamous Cell Carcinoma of the Lung." V Foundation, $600,000.

Fields, A. (2006 TSP), "Protein Kinase C Signaling Mechanisms in Cancer." National Institutes of Health. $1,292,414.

Goldberg, J. (2005 NIR), "Retinal Scaffolds: Synaptic and Stem Cell Integration." National Eye Institute. $382,486.

Haura, E. (2001 NIR), "Evaluate the Ability of an Anit-IL6 Antibody to Down-Regulate Stat3 & Inhibit in vitro & in vivo Lung Cancer Growth, Angiogenesis & Metastasis." Centocor, Inc. $189,508.

Hu, B. (2007 Bridge), "Translational Complex Aggregation after Brain Ischemia." National Institutes of Health. $328,576.

Lee, D. (2006 TSP), "Health and Economic Aspects of Ocular Disease in the US." National Eye Institute. $229,500.

Liebl, D. (2001 NIR), "Molecular Mechanisms of Adult Neurogenesis Following TBI." National Institute of Neurological Disorders & Stroke. $60,000.

Liebl, D. (2001 NIR), "Ephrins Regulate Stem Cell Proliferation Following TBI." National Institute of Neurological Disorders & Stroke. $296,958.

Lincoln, J. (2007 NIR), "Molecular Regulation of Heart Valve Development and Disease." National Institutes of Health, $382,500.

Luesch, H. (2006 NIR), "Chemistry and Biology of Largazoles." National Cancer Institute. $654,882.

Mohapatra, S. (2007 TSP), "Production of Platelets for Hematopoetic Stem Cells using 3-D Smart Scaffolds." Office of Naval Research. $971,000.

Mohapatra, S. (2007 TSP), "Targeted Delivery of siRNA Nanoparticles to Prevent HIV-1 Trasmission." National Institutes of Health. $162,039.

Mohapatra, S. (2007 TSP), "Matching Grant to NIH Grant." Florida High Tech Corridor. $162,039.

Mohapatra, S. (2007 TSP), "Nanomedicine Research Center Core (NRCC)." National Institutes of Health. $1,329,000.

Perez, M. (2008 Bridge), "Ischemic Preconditioning: Mechanisms of Neuroprotection." National Institute of Neurological Disorders and Stroke. $1,673,440.

Powers, S. (2001 IIR), "Mechanical Ventilation and Diaphragmatic Oxidant Injury." National Institutes of Health. $1,241,644.

Radisky, E. (2008 NIR), "Development of Highly Selective MMP-9 Inhibitors for Breast Cancer Therapy." Bankhead-Coley Cancer Research Program, $375,000.

Radisky, E. (2008 NIR), "Development of Highly Selective MMP-9 Inhibitors for Breast Cancer Therapy." Department of Defense, $565,074.

Rollison, D. (2006 NIR), "Epidemiologic Pilot Study of MDS Incidence in Florida." University of Florida. $64,493.

Salathe, M. (2005 TSP), "Newly Independent Faculty Recruitment and Support for Pulmonary." National Heart, Lung, and Blood Institute." $1,083,822.

Salathe, M. (2005 TSP), "Phosphorylation of Ciliary Target Proteins." National Heart, Lung, and Blood Institute." $1,530,000.

Salathe, M. (2005 TSP), "Mucociliary Function in Chronic Bronchitis." National Heart, Lung, and Blood Institute." $1,912,000.

Siegel, E. (2005 NIR), "Defining Novel Biomarkers for Cervical Cancer Etiology and Progression by Quantitative Epigenomic Analysis." National Cancer Institute. $192,290.

Simmons, V. (2008 NIR), "Development of a Tobacco Cessation Program for People with Disabilities." University of Florida. $78,414.

Trapido, E. (2001 IIR), "State of Florida Aids Surveillance." Florida Department of Health. $166,067.

Webster, K. (2007 TSP), "JNK exacerbates ischemia/reperfusion injury in hyperglycemic subjects." National Heart Lung & Blood Institute. $956,250.

Webster, K. (2007 TSP), "Mechanisms of action and activation of the death-inducing protein Bnip3." National Heart Lung & Blood Institute. $1,147,500.

Willing, A. (2007 Bridge), "Trophic Effects of CordBlood in Aging Brain." Johnnie Byrd Alzheimer Center. $80,000.

Willing, A. (2007 Bridge), "Expanding the Therapeutic Window to treat Stroke." National Institutes of Health. $275,000.

Willing, A. (2007 Bridge), "Use of Pioglitazone in Treating Stroke at Delayed Time Points." Takeda Pharmaceuticals. $180,000.

Yu, H. (2007 TSP), "Effect of Aging on Anti-Atherosclerosis Role of Progenitor Cells." American Heart Association Florida Affiliate. $170,000.

Since October 2008, current and past grantees reported $11.1 million in awards that are indirectly related to research findings from projects funded by this Program. However, the James & Esther King award enhanced their competitiveness in earning this additional funding. Grants are presented in alphabetical order by last name of the principal investigator, with the King award year and type listed in parentheses.

Bishop, M. (2004 NIR), "Neurobiological Mechanisms of Body Based Intervention for Musculoskeletal Pain." National Institute of Arthritis and Musculoskeletal and Skin Diseases, $434,740.

Chan, S. (2007 NIR), "Roles of Alpha-Synuclein in Stroke Induced Brain Damage." National Institute of Neurological Disorders and Stroke. $204,900.

Cogle, C. (2005 NIR), "Defining the Human Hemangioblast." National Institute of Diabetes and Digestive and Kidney Disease." $409,800.

Elliot, S. (2001 NIR), "Estrogen Deficiency and Renal Disease in Aging Women." National Institute on Aging. $1,361,700.

Gerend, M (2007 NIR), "Using Message Framing to Promote HPV Vaccination." National Cancer Institute. $146,000.

Goldberg, J. (2005 NIR), "Retinal Scaffolds: Synaptic and Stem Cell Integration." National Eye Institute. $764,972.

Hochwald, S. (2001 NIR), "FAK and IGF-1R Interaction in Pancreatic Cancer Survival." National Cancer Institute. $276,604.

Isgor, C. (2005 NIR), "Individual Differences in Relapse to Nicotine." National Institute on Drug Abuse. $213,750.

Judge, A. (2008 NIR), "Heat Shock Proteins and Disuse Muscle Atrophy." National Institute of Arthritis and Musculoskeletal and Skin Diseases. $219,750.

Judge, A. (2008 NIR), "The Role of Heat Shock Protein 70 Overexpression on the Recovery of Muscle Mass and Function Following Cast Immobilization in Old Rats." University of Florida Pepper Institute. $46,616.

Mohapatra, SS. (2004 NIR), "Targeting of Curcumin-genistein nanocomplexes for Treatment of Prostate Cancer." National Cancer Institute. $158,829.

Vazquez-Padron, R. (2006 NIR), "Genetics of In-Stent Restenosis: The Mouse to Human Strategy." National Heart, Lung and Blood Institute. $418,708.

Zhai, G. (2007 NIR), "Mechanisms of Neuronal Maintenance and Protection." National Institute of Neurological Disorders and Stroke. $1,637,500.

Appendix D.
Abbreviated Abstracts of 2009 Grant Awards

The following is a list of grants awarded in 2009. The grants are listed in alphabetical order by Principal Investigator name. For a complete description of grant types, see page 13.

Ames, Steven
2009 RC1
Mayo Clinic
$716,453

Integrated Intervention for Cigarette Smoking and Binge Drinking in Young Adults

Despite the very high prevalence of smoking in young adults, little effort has been made to address the needs of this group. Substantial evidence links high-risk styles of alcohol use, such as binge drinking, to smoking cessation treatment failure. Related to this, evidence supports the hypothesis that a decrease or cessation of binge drinking should be associated with a decrease or cessation of tobacco use. Thus, an innovative approach with young adult smokers who are binge drinkers is to design an intervention focused on eliminating both of these behaviors. This study will explore the intriguing possibility that an intervention that integrates these two treatment elements might be more effective for smoking cessation than treating cigarette smoking independent of binge drinking. An important additional benefit of this treatment is its potential to reduce binge drinking, which is a high-risk form of alcohol consumption. To our knowledge, we are the only group that is working to explore this innovative line of research.

Aponick, Aaron
2009 NIR
University of Florida
$374,451

Studies on Spirastrellolide A to Probe the Significance of PP2A in Tumorigenesis

Despite many years of intensive research, cancer continues to plague our society and affect the lives of an incredible number of Americans. At this stage, many question whether it will ever be possible to find a cure. To increase the likelihood, it is necessary to study novel chemotherapeutics and previously unexplored targets for these agents. Nature is an incredible source of potential leads, with new natural product molecules identified regularly. These new compounds often show promising anti-cancer activity, but are only available from natural sources in extremely small quantities. Synthetic organic chemists bridge the gap between the identification of these compounds and the ability to study them as potential treatments. The research outlined in this grant aims to study the natural product spirastrellolide A. This compound is a potent and selective inhibitor of enzymes involved in cell signaling, which is an important target for chemotherapy. Spirastrellolide A is an extremely complicated molecule and can only be prepared in exceedingly small amounts by the current state-of-the-art organic synthesis methods. The goals of this project are to design efficient new synthetic methods for the synthesis of Spirastrellolide A (which will also be applicable in the synthesis of many other chemotherapeutics), to prepare the compound, and to study its biological activity. The long-term objective is to find simplified analogues to be used as pharmaceuticals.

Barrientos, Antoni
2009 RC1
University of Miami
$660,000

Slowing Degenerative Processes by Bolstering Cellular Bioenergetics

In aerobic conditions, most energy produced by eukaryotic cells is generated by the mitochondrial respiratory chain and oxidative phosphorylation system (OXPHOS). A defect in OXPHOS leads to diseases involving degeneration of affected organs. In most cases, mitochondrial disorders are of genetic origin. However, they can also result from exposure to chemical pollutants such as those present in tobacco leaves and smoke. Chronic smoking produces inhibition of cytochrome c oxidase (COX), a crucial enzyme of the OXPHOS system, and increased generation of reactive oxygen species (ROS). COX disturbance and ROS contribute to the deleterious cellular oxidative processes common in cardiovascular disease and favor mutagenic events leading to cancer development. Tobacco smoking is also a known risk factor for certain mitochondrial disorders. Currently, there is not effective treatment for mitochondrial disorders of either genetic or environmental origin. Our hypothesis is that impaired OXPHOS activity can be boosted to improve energy output and cellular health. The purpose of this grant is to develop an effective therapeutic intervention for these disorders.

Beaver, Thomas
2009 RC1
University of Florida
$772,503

Does Nesiritide Provide Renal Protection by Attenuating the Inflammatory Response in Cardiac Surgery?

Smoking and tobacco have been implicated in the development of both coronary artery disease of the heart and the development of aneurysms in major vessels. Surgery is often used to treat these conditions with the help of a cardiopulmonary bypass machine, but there is always a small risk of kidney injury. Patients that develop kidney injury after surgery have worse survival and some end up requiring dialysis. In fact, more than half of those patients that require dialysis die shortly after their surgery. Currently, there are no drugs on the market to prevent kidney injury after surgery. However, there is recent evidence that a group of compounds called "natriuretic peptides" may provide kidney protection. This project focuses on how natriuretic peptides confer kidney protection during cardiovascular surgery. This is a pilot study focusing on patients undergoing "thoracic aortic surgery" who are at the highest risk for kidney injury. A better understanding of the protective mechanisms of natriuretic peptides in these patients will be translated to make surgery safer for the hundreds of thousands of patients that undergo cardiovascular surgery each year because of tobacco-related cardiovascular disease.

Bennett, Eric
2009 RC1
University of South Florida
$713,117

Regulated and Aberrant Glycosylation Modulate Cardiac Excitability

Heart disease is the number one cause of adult death, with millions of people suffering from cardiac arrhythmias. Tobacco use increases susceptibility to cardiac arrhythmias. Normal heart rhythm is produced by the orchestrated conduction of electrical signals (action potentials, AP) throughout the heart. Action potentials are produced by the regulated activity of voltage-gated ion channels. Slight changes in channel activity can alter AP waveform and lead to arrhythmias. Recently we showed that regulated glycosylation likely alters cardiac conduction. The goal of this project is to test the hypothesis that regulated and aberrant glycosylation modulate cardiac electrical signals using a series of methods at several organizational levels from whole animal to molecular. If the hypothesis is viable, then a novel mechanism for control and modulation of cardiac function would be described. Cardiac function would then be studied in light of this newly described mechanism, including questioning the role of tobacco in modulating cardiac function through changes in the glycan structures produced by the heart.

Bixby, John
2009 RC1
University of Miami
$663,262

Combination Therapy in SCI: Proof-of-Concept for New Compounds and Candidate Genes

Long-term smoking or other uses of tobacco lead to a variety of health problems; one of the most serious of these is stroke. Smoking is a strong risk factor for strokes, increasing the overall risk of these debilitating events by two-four fold. Stroke refers to a variety of processes that cause a loss of normal blood flow to the brain. This loss of blood flow in turn leads to the irreversible loss of some nerve cells, and the disconnection of other nerve cells from their normal brain circuits. The loss of connections in the brain can result in paralysis, weakness, confusion, loss of speech, and many other serious deficits. Although stroke patients can recover some function with rehabilitation, at present some losses are permanent. Such permanent deficits could be reversed if we could find a way to cause injured nerve cells to sprout new connections and regenerate the long fibers (axons) that allow them to communicate with other structures, such as muscles and the spinal cord. This grant is designed to test whether ideas we have developed in tissue culture (growing nerve cells in lab dishes) can be translated to improvements in the regeneration of axons in a living mouse. We will test whether new chemical compounds we have identified will be able to promote regeneration of damaged brain axons. In parallel, we will test whether causing nerve cells to make regeneration-promoting proteins, or to stop making regeneration-inhibitory proteins, will help them regenerate.

Borlongan, Cesar
2009 Bridge
University of South Florida
$110,000

Preclinical STEPS Consortium

Bone marrow derived progenitor cells have properties that make them highly suitable as donor cells for restorative therapy. Theradigm, Inc., and SanBio, Inc., have the proprietary rights to specific progenitor cells derived from bone marrow and have developed manufacturing techniques to make them available for clinical use. Our research team has a collaborative relationship with these companies, which will supply these cells to us. Our preliminary data in rodents indicate that transplantation of these cells stands as a promising therapy for ischemic stroke. In order to develop the utility of these cells fully for clinical stroke, we propose a series of experiments to serve as the preclinical basis for proceeding with transplantation of these cells in ischemic stroke patients. This grant establishes the Preclinical STEPS (Stem cell Therapeutics as an Emerging Paradigm for Stroke) Consortium, comprised of three expert stroke laboratories, a Data Coordination Center, and a clinical steering committee. The overarching goal is to provide the optimal cell transplantation regimen (including dose, route, and timing post-stroke) for each bone marrow derived progenitor cell type that will produce an effective and safe cell therapy in rodent models of adult ischemic stroke. It is imperative for clinical translation that these cells be tested in multiple models of focal stroke, in two species, and in multiple laboratories. Because stroke is a leading cause of death and disability in the U.S. and around the world, the preclinical demonstration of efficacy and safety of cell therapy, along with the appropriate guidelines, should enhance the success of this experimental treatment in the clinic.

Boulton, Michael
2009 RC1
University of Florida
$650,422

Targeting the Unfolded Protein Response as an Adjunct to Treatment of Ocular Neovascularization

Smoking is a major risk factor for the visual loss caused by aberrant neovascularization (proliferation of blood vessels in tissue not normally containing them) in both age-related macular degeneration and diabetic retinopathy. This study will challenge the current treatment paradigm of targeting the extracellular angiogenic factor (substance that causes growth of new blood vessels), vascular endothelial growth factor (VEGF). Current treatments ignore the critical contribution of the intracellular VEGF signalling pathway; the results are often not sustainable or complete, and many patients do not benefit significantly. We have identified that the "unfolded protein response" (UPR) pathway is responsible for activating the intracellular VEGF signaling pathway. This intracellular pathway overrides the extracellular VEGF pathway, which is the current clinical target. Based on our preliminary data, we predict that co-administration of an agent that blocks the UPR together with a conventional inhibitor of extracellular VEGF, will greatly improve the clinical outcome of patients with neovascularization.

Cogle, Christopher
2009 SIG
University of Florida
$238,595

Fluorescence Activated Cell Sorter for Treatment of Tobacco-Related Diseases

Fluorescence-Activated Cell Sorting (FACS) is an essential technology for translational research where individual cells must be studied in large numbers, particularly when the source material is a mixture of cells, such as patient tissues or mixed cell cultures. A number of investigators at the University of Florida (UF) Health Sciences Center are testing new cellular therapies for the treatment of tobacco-related diseases such as cardiovascular disease, limb ischemia, bone marrow failure, and cancer. Cellular therapies for these diseases require cell collection, processing, storage, and infusion. The cells are administered with intent to repair tissues damaged by tobacco toxicity. A FACS system will greatly benefit the translational research work by UF physician-scientists by endowing them with the capability to adequately characterize harvested, processed, cryopreserved, and infused cells intended for investigational therapies. Careful evaluation of cells is required by the Food and Drug Administration (FDA) and for scientific reporting purposes. Thus, a FACS system is a critical piece of equipment that is essential for the success of physician-scientists at UF and Shands Hospital.

Dang, Stuti
2009 TTCP
University of Miami
$99,999

A Novel Fully Integrated Mobile Management Solution Using Cell Phone Technology for Heart Failure

Disease management programs have shown that compliance with medications and diet improves longevity and decreases the need for hospitalization in patients with heart failure (HF). The effectiveness of disease management programs is often limited by manpower and budgetary issues. Mobile phone networks provide a unique opportunity to address these limitations by being ubiquitous, offering the capability for automated text and voice monitoring and reminders, and the potential for data gathering. GenerationOne (Gen1) working with UM investigators has developed a protocol for a unique automated mobile phone–based system that enables daily monitoring for improving self-care and care coordination for HF. The goal of our application is to develop, implement, and evaluate the usability and utility of this mobile-phone text-messaging technology among HF patients. In this grant, we will develop the mobile phone system, test its usability (reliability, acceptability, and feasibility), and conduct a randomized controlled trial to evaluate its utility with regard to patient self-care efficacy and satisfaction. This project will help gather pilot data to apply for a larger grant to develop an interactive voice-response Gen1 system using cell phones. This project will pave the way for more studies and efforts toward developing GenerationOne products and services for effective and efficient population-based chronic disease management.

Evans, David
2009 NIR
H. Lee Moffitt Cancer Center & Research Institute
$365,908

Genetic Moderation of Nicotine-Induced Cognitive Enhancement

Smoking tobacco remains the top preventable cause of disease and death in our society. Nicotine enhances attentional control. This enhancement may be greater among individuals who have attentional deficits. Therefore, the acute effects of nicotine on attention during the earlier stages of nicotine use may result in greater reinforcement among individuals who are lower in attentional control. Differences at the molecular genetic level may in part underlie this association. We will examine genetic variants associated with neurotransmitters involved in both smoking/nicotine and attentional control. In order to avoid nicotine withdrawal as an alternative explanation, nonsmokers will be given nicotine patch at the beginning of one experimental session and placebo patch during the other. Participants will complete tasks that assess attentional control. Brain activity data associated with performance on these tasks will also be examined. We hypothesize that individuals with genetic variants indicative of reduced attentional control will show greater improvements on attentional control following nicotine relative to placebo patch. The information gained from this research will contribute to our understanding of nicotine use in relation to attentional deficits. We expect to utilize the information gained from this research to guide the development and evaluation of smoking cessation treatment programs.

Fan, Z. Hugh
2009 Bridge
University of Florida
$141,184

Two-Dimensional Electrophoresis Device for Biomarker Detection

Proteomics, the large-scale study of proteins, is one of the emerging tools for drug discovery and medical diagnostics. Two-dimensional gel electrophoresis is one of the most potent methods in proteomics studies. The purpose of this grant is to develop a lab-on-a-chip device that will improve the performance of conventional gel electrophoresis. Two separation mechanisms will be integrated with microvalves and other components in the device. The device will address the key drawbacks of the current method, including poor reproducibility and time-consuming processes. The impact of the research could be significant because gel electrophoresis is widely used in biological laboratories. After the platform is successfully implemented, it could become a method for studying the association between biomarkers and diseases including those related to tobacco use. After the biomarkers are established and clinically validated, the platform could also become a rapid, quantifiable diagnostic tool to help physicians determine the seriousness of diseases based on the level of the biomarkers present in patients' bodily fluids.

Gabrilovich, Dmitry
2009 TSP
H. Lee Moffitt Cancer Center & Research Institute
$1,000,000

Myeloid-Derived Suppressor Cells in Tobacco-Related Cancers

Cigarette smoke contains an extremely high concentration of oxidants together with a number of known carcinogens, and the risk of developing lung cancer does not disappear after smoking has been discontinued. Tissue inflammation is one of the major factors responsible for the development and progression of tumors associated with tobacco use. The local inflammation initiated by cigarette smoke persists after patients have stopped smoking. A main characteristic of inflammatory response is accumulation of activated myeloid cells in tissues. In recent years, these cells were identified as myeloid-derived suppressor cells (MDSC). These cells produce reactive oxygen and nitrogen species that result in tissue damage. In addition to tissue damage, MDSC were shown to exert profound immune suppressive effect. Dramatic expansion of MDSC was found to be critically important for failure of cancer vaccines. This grant focuses on a multi-disciplinary approach to understanding the biological role and therapeutic regulation of MDSC in tobacco-related cancers. It combines efforts from investigators in different fields and with unique resources available for investigation of the role of MDSC in cancer progression and the therapeutic regulation of MDSC. The ultimate goal is to gain a better understanding of the mechanism of tumor development and progression associated with tobacco use and to develop novel therapeutics.

Hare, Joshua
2009 SIG
University of Miami
$500,000

Fixed-Base Biplane Imaging Laboratory for Experimental Models and Preclinical Therapeutic Studies in Cardiovascular Diseases Caused by Tobacco

Heart disease and stroke are the first and third leading causes of death in the United States, respectively, and smoking causes all forms of cardiovascular disease. Unfortunately, once damaged by lack of blood flow, the heart muscle, the brain, and other organs are irreversibly scarred. The University of Miami Interdisciplinary Stem Cell Institute (ISCI) conducts research in tobacco-related diseases and has an established track record in studying stem cell therapy for cardiovascular damage. The purpose of this shared instrument grant is to obtain a Cardiovascular Angiography System, which consists of dual x-ray imaging devices and computer systems for collection of digital x-ray images for preclinical research in animal models. The instrument is essential to the conduct of our research in the minimally invasive delivery of stem cells to diseased tissue. This instrument is shared by successful cell-therapy programs, which hold the promise of groundbreaking cures for tobacco-related cardiovascular diseases.

Ibrahim, El-Sayed
2009 NIR
University of Florida
$367,111

Evaluation of the Relationship between Right Ventricular Myocardial Mechanics and Pulmonary Artery Vessel and Flow Dynamics in Pulmonary Artery Hypertension by MRI

Pulmonary arterial hypertension (PAH) is a challenging pathological condition characterized by progressive elevation in the blood pressure of the arteries of the lung, which could lead to substantial morbidity and mortality from right ventricular (RV) failure if not treated properly. The direct effect of tobacco smoking on PAH has been established. Smoking causes progressive increase in pulmonary arterial (PA) pressure. RV is affected by impaired diastolic function due to elevated PA pressure. However, the relationship between RV dysfunction and PA compliance has not been fully investigated. The purpose of this grant is to evaluate this relationship using state-of-the-art, high-field magnetic resonance imaging (MRI). MRI with its superior tissue contrast, high spatial and temporal resolution, and non-invasive nature is an important modality for assessment of cardiac function. In the first stage of this grant, computer simulations will be conducted to optimize the imaging parameters. Volunteer scans will then follow to develop the imaging protocol. Different MRI techniques will be optimized for measuring RV function and PA compliance. Finally, PAH patients will be recruited and imaged with the developed MRI exam to measure RV strain, volume, and filling rate, as well as PA stiffness and flow patterns. A thorough statistical analysis will be conducted on the results to help further understand the relationship between RV dysfunction and PA compliance in PAH. The results of this study would allow for a comprehensive MRI cardiac exam of PAH in the future.

Jent, Jason
2009 NIR
University of Florida
$353,215

The Effectiveness of the Reducing Environmental Tobacco Exposure Program within a Healthy Steps for Young Children Pediatric Model: A Randomized-Controlled Trial

The long-term primary objective of the University of Miami's Reducing Environmental Tobacco Exposure Program (RETEP) is to reduce young children's exposure to environmental tobacco smoke (ETS) by using a motivational intervention within Healthy Steps pediatric primary care practices. RETEP's aims include: training program staff on ETS screening and RETEP intervention protocol and evaluating the effects of ETS screening and RETEP intervention on children's exposure to ETS, child health, and parent smoking rates. The aims reflect the program's intentions to reduce children's exposure to ETS and ETS-related child illnesses (e.g., respiratory illnesses). Children's exposure to ETS will be measured through child urine samples and parent report. The intervention's impact on child health will be directly measured by medical chart review. The intervention aims to reduce parent-smoking rates indirectly by delivering the ETS reduction intervention, which focuses on: informing parents about ETS exposure effects on children; assessing parents' willingness to reduce their child's exposure to ETS; assessing barriers to change; and assisting parents in making individualized ETS reduction plans. Specifically, these personalized plans will focus on decreasing ETS smoke in the home, car, and if the parent is ready, a referral and resource guide for smoking cessation will be provided. The main focus of the intervention will be improving the health of children exposed to ETS.

Kanai, Masayuki
2009 NIR
H. Lee Moffitt Cancer Center & Research Institute
$374,998

Molecular Dissection of the RockII-dependent Regulation of Centrosome Duplication

Aneuploidy (chromosome loss and/or gain), which plays a critical role in carcinogenesis with multiple genetic alterations, is commonly found in cancer cells. Chromosome loss/gain occurs as the consequence of chromosome segregation errors during cell division, in which the organelle called centrosome plays a critical role: two centrosomes direct the accurate separation of duplicated chromosomes. Thus, the presence of more than two centrosomes (centrosome amplification) increases the frequencies of chromosome segregation errors, leading to aneuploidy. Indeed, centrosome amplification is frequently observed in cancer cells. Centrosomes duplicate once before cell division, and centrosome amplification is primarily caused by uncontrolled duplication of centrosomes. Thus, it is important to understand how centrosome duplication is controlled, and how loss of the control results in centrosome amplification. We have recently identified the protein named ROCK II. This protein plays a key role to initiate centrosome duplication, and aberrant activity of it leads to centrosome amplification. In this grant, we will investigate how ROCK II controls centrosome duplication and how ROCK II is controlled by other cancer-associated proteins for the initiation of centrosome duplication. Since centrosome duplication may be a superior target for cancer prevention/therapy, the findings from this grant will provide valuable information toward the development of such a protocol.

Lang, Jason
2009 NIR
Nemours Children's Clinic
$374,901

Environmental Genetics (En-Gen): Effect of Environmental Tobacco Smoke and Genetic Variation on Leukotriene Production in Asthmatic Children

Environmental Tobacco Smoke (ETS) imposes an enormous disease burden, particularly among vulnerable groups such as children and those with respiratory conditions such as asthma. Asthmatic children exposed to ETS are at risk for accelerated loss of lung function and worsening disease severity, and may be at increased risk for death, though the precise mechanisms remain unclear. Leukotrienes are molecules made in the body that can cause inflammation. Since active smoking increases leukotriene production, leukotriene-driven inflammation may be a critical component of ETS-induced asthma. This grant is an ancillary study to a multi-center pediatric asthma study conducted by the American Lung Association Asthma Clinical Research Centers (ALA-ACRC). We will determine associations among ETS exposure, leukotriene production, and asthma severity. We expect that ETS exposure will increase both production of leukotrienes and asthma severity. We will also determine associations between leukotriene gene alterations, leukotriene production, and asthma symptoms. Variations in certain genes may alter ETS-induced leukotriene production and resulting asthma severity. This study may better delineate how ETS worsens asthma in children. Common gene variations may place certain individuals at severe risk of ETS-lung injury. Genetic analysis paired with data on ETS exposure and asthma severity may greatly contribute to the goal of improved and personalized asthma care.

Lewin, Alfred
2009 SIG
University of Florida
$191,390

Spectral Domain Instrumentation for Macular Degeneration Research

Age related macular degeneration (AMD) is the leading cause of blindness among the elderly in the United States. Smoking is the most important environmental risk factor for AMD. This project team consists of a group of five scientists collaborating to study this disease and to develop a cure using mouse models of macular degeneration. We are developing both stem cell and gene therapy approaches to treat the disease. Grant funding is for the purchase of a spectral domain optical coherence tomography (SD-OCT) instrument to obtain high-resolution images of the retina in living animals. Optical coherence tomography is a method for acquiring and processing optical signals in complex media. It permits the production of high-resolution, 3-dimensional images from within biologic tissues. In SD-OCT, a full-depth scan can be acquired within a single exposure. This method permits cross-sectional analysis of the retina with resolution that rivals that of microscopy, allowing us to monitor the course of disease and the efficacy of treatment in one cohort of living animals. The instrument provides not only the latest spectral domain OCT capability but also multiple other ocular imaging methods that permit detection of leaking blood vessels characteristic of late-stage AMD and dead or dying photoreceptors. Currently we have no other instrument that will perform these tasks at high resolution.

Martin, Anatole
2009 RC1
University of Florida
$684,484

Inspiratory Muscle Strength Training in Ventilator Dependent Patients

Mechanical ventilators are life-saving devices for acutely ill patients unable to breathe without assistance; however, these machines may weaken the breathing muscles, making it difficult for patients to breathe without ventilator support after their acute illness has resolved. Cigarette smoking has been shown to increase the time patients need support from ventilators compared to nonsmokers. For this study, the researchers are initiating a respiratory muscle strength-training program on patients soon after they start receiving mechanical ventilation in order to compare their outcome to patients that receive a sham treatment. It is hoped that by starting breathing muscle rehabilitation activities very soon after starting mechanical ventilation, patients will require fewer days of mechanical ventilation and will be easier to wean from mechanical ventilation. Lowered healthcare costs for these patients could also result.

Mbah, Alfred K.
2009 NIR
University of South Florida
$374,733

Effect of Passive Smoking on Risk for Antenatal and Post-partum Depression

Depression in the mother is an important public health concern because it could lead to the mother killing herself and her baby. Secondhand tobacco smoke has been associated with depression in the general population, but its relationship to maternal depression is poorly understood. The aim of this grant is to assess the effects of secondhand smoking on antenatal and post-partum depression. We intend to screen and recruit actively non-smoking pregnant women early in pregnancy at the Genesis Clinic in Tampa. We will screen them to establish secondhand smoking exposure using a questionnaire and testing for the presence of a substance (cotinine) in maternal urine and cord blood. At first and subsequent visits, we will look for symptoms of depression using a validated questionnaire, the Edinburgh Post-partum Depression Scale (EPDS). At subsequent study visits, mothers will be screened again to assess any changes in symptoms of depression and smoking status. This study is significant because it addresses an important health effect that could be caused by passive smoking, which is a preventable environmental factor. Additionally, the proposed use of a biomarker to establish secondhand smoking status is innovative.

McLaughlin, Mark
2009 SIG
University of South Florida
$498,000

Acquisition of a High-Throughput 500 MHz NMR for the Characterization of Potential Anti-Cancer and Anti-Stroke Therapeutics

Drug design and synthesis is very much analogous to architecture and construction, respectively. An architect designs a building to fit a 3D space to serve its function as a home or a place of business and the resulting construction techniques will hopefully produce a robust building that will survive Florida's weather for at least 100 years. Drug design involves the design of molecules to fit a defined three-dimensional space, which is usually a protein-binding site. The synthesis of molecules to fit the protein-binding site is complicated by numerous additional constraints. The designed drug must fit the protein-binding site with at least competitive binding as compared with the natural molecule fitting that binding site. Instead of needing to survive Florida storms, the drug molecules must be stable for storage and for some period of time in the body of the patient. These and other reasons require that several structurally related molecules be prepared and tested to determine which molecules will best fit the protein-binding site. Nuclear Magnetic Resonance (NMR), which is analogous to MRI, is the best method of structurally characterizing molecules, and the high-throughput NMR instrument obtained through this grant will expedite the structural analysis of drug candidates. This instrument will therefore speed our progress in finding drug candidates to treat tobacco-related diseases such as cancer and stroke.

Miller, Brian
2009 NIR
Florida State University
$375,000

Mechanism of Kinetic Cooperativity in Monomeric Human Glucokinase

Diabetes is a vastly understated consequence of tobacco use. Indeed, smoking more than doubles the risk of developing type 2 diabetes. Unlike other diabetes risk factors, the diabetes-promoting effects of tobacco act independently of an individual's weight or fitness level. Nicotine appears to provide the key link between tobacco use and diabetes. Progressive and persistent exposure to nicotine results in a slow deterioration in the body's ability to process glucose. When normal glucose processing is abolished, diabetes can result. The objective of this grant is to understand how glucose is processed within the body and how nicotine acts to disrupt this process. In particular, our work focuses on the mechanism of action of a single human protein called glucokinase. Glucokinase is a key regulator of glucose homeostasis, yet much is unknown about how this protein responds to changing glucose levels. Importantly, glucokinase has emerged as an attractive therapeutic target for diabetes. In the last five years, several drugs have been developed that target glucokinase, and several have been shown to be effective at modulating blood glucose levels in animal models. The successful completion of this grant will provide critical new information about the role of glucokinase in tobacco-associated diabetes. This information has the potential to significantly impact future efforts to design glucokinase-targeted therapeutics for diabetes and hyperinsulinemia.

Mohapatra, Shyam
2009 SIG
University of South Florida
$499,994

4-D Live Cell Imaging System

Rapid development of safer and more effective drugs for cancers and other tobacco-related diseases requires better detection methods and hence the application of the newest technology. Disease cells are not static. They grow and change with time and often migrate to other organs. One of the ways researchers study these cells is through the use of special imaging systems combining a sophisticated microscope, ultrasensitive camera, and dedicated computer software. This system allows scientists to look inside the cells and see which proteins and enzymes are being made. Also, the extreme sensitivity of the detector means that diseased cells may be detectable at a much earlier stage so that treatment can begin when the chances of survival are greatest. USF College of Medicine has invested recently in establishing a microscopy core and founding a Nanomedicine Research Center to advance translational medicine. However, it lacks a state-of-the-art live cell imaging system. This shared instrument will help a number of researchers at the College of Medicine advance their projects more quickly and acquire data for publication, thus increasing the chances of federal research funding.

Monteiro, Alvaro
2009 Bridge
H. Lee Moffitt Cancer Center & Research Institute
$200,000

BRCA1 Status as a Marker of Clinical Outcomes in Lung Cancer

The main agents used for chemotherapy for lung cancer aim to prevent the growth of cancer cells. However, many patients suffer the serious side effects without experiencing a significant disease response. Therefore, the identification of markers that can predict response to specific drugs is a top priority in lung cancer management. Recently we provided results indicating that the status of two nuclear proteins can predict response to some chemotherapy drugs. Conspicuously absent from this predictive panel is a marker to predict response to drugs (taxanes) that target fibers used by the cells to divide genetic material. We hypothesize that the status of a protein involved in cancer development (BRCA1) correlates with response to taxanes and can be developed as a predictor of drug response. Using a combination of studies in cell lines and in tumor tissues, we will determine the extent to which the status of BRCA1 correlates to response. This is significant because it is expected to fill in a gap in the treatment of lung cancer. The development of a panel of reliable predictors of response to drugs commonly used has the potential to change clinical practice and bring us closer to our long-term goal of delivering effective personalized medicine. Our long-term goal is to provide a panel of markers that can be evaluated in the biopsied material from the individual tumor. This information could then be used to predict which drugs will be more or less effective for an individual patient.

Moy, Vincent
2009 SIG
University of Miami
$489,496

Acquisition of a Nikon A1-R-SI Confocal Laser Microscope for an Integrated Confocal-AFM System

This confocal laser microscope is part of the University's Ultramicroscopy Core Facility and is a fully automated confocal imaging system, capable of capturing high-quality confocal images of cells and molecular events at high speed and enhanced sensitivity. The Nikon A1-R-SI in combination with an existing Asylum Research MFP-3D-BIO Atomic Force Microscope (AFM) forms a state-of-the-art, integrated confocal-AFM system. The integrated system is capable of simultaneously acquiring confocal images and AFM measurements of surface topography and cell elasticity from live cells. It is a versatile instrument that combines molecular resolution imaging and piconewton force measurements with the specificity of confocal microscopy. The integrated confocal-AFM system is shared by more than 25 users from 3 major user groups (Drs. Moy, Li, and Goldberg) and 3 minor user groups (Drs. Cote, Cheung and Leblanc). The projects that this shared instrument helps to support have relevance in the diagnosis and/or treatment of tobacco-related diseases including atherosclerosis, skin cancer, and stroke.

Najmunnisa, Nasreen
2009 NIR
University of Florida
$375,000

Eph-A2 Signaling in Tobacco Smoke Induced Bronchial Airway Epithelial Injury

Tobacco smoke is the major risk factor for the development of chronic obstructive pulmonary disease (COPD). COPD is characterized by chronic inflammation of the airways and progressive destruction of lung parenchyma (the functional parts of the lung). The destruction of lung parenchyma is associated with death of bronchial airway epithelial cells (BAEpCs), which leads to emphysema. During tobacco smoking, BAEpCs are the first cells to come in contact with inhaled smoke in the lungs. This tobacco smoke exposure leads to BAEpC shedding and cell death, which compromises epithelial barrier function. However, very little is known about exactly how this happens, particularly the identity and contribution of cell surface proteins that regulate these events in COPD. We have identified a marker protein that is expressed on the surface of BAEpCs called the Erythropoietin producing hepatocellular (Eph) receptor (EphA2) that plays a key role in tobacco smoke-induced BAEpC barrier dysfunction. The overexpression of receptor EphA2 has been implicated in cell differentiation and growth as well as the regulation of cell migration, adhesion, and cell death. This research aims to study the effect of tobacco smoke on BAEpCs' EphA2 signaling by using a mouse model of COPD we have developed. Understanding the mechanisms of EphA2 receptor signaling induced by tobacco smoke may help establish novel therapeutic strategies to treat COPD patients.

Najmunnisa, Nasreen
2009 RC1
University of Florida
$587,689

Intratumoral Gene Therapy (ITGT) in Mouse Model for Lung Cancer

Tobacco smoke is a major risk factor for the development of lung cancer and accounts for 87 percent of lung cancer-related deaths in the U.S., and 80 percent of deaths are due to Non Small Cell Lung Cancer (NSCLC). The prognosis of patients with advanced or metastatic NSCLC is poor. Despite significant advances in diagnosis and treatment, little improvement has been seen in NSCLC mortality. Recently, Intratumoral Chemotherapy (ITC), a direct local delivery of chemotherapeutic drugs, has shown promise. However, toxicity and high dosage of chemotherapeutic agents used for treatment are a limitation. Moreover, these drugs damage indiscriminately, affecting cancerous as well as normal tissues. Thus, a novel therapeutic strategy that targets only malignant tissue sparing normal tissue has become an urgent issue. Targeting the tumor and sparing the normal tissue is the goal of this project. We have developed a novel method, Intratumoral Gene Therapy (ITGT) to target only tumor tissue by using EphrinA1 loaded albumin microspheres in mice bearing NSCLC tumors. The data obtained from this study offers an exciting avenue for the development of therapeutic drugs that may help treat NSCLC patients in Florida.

O'Malley, Kerri
2009 NIR
University of Florida
$375,000

Interleukin-1 Beta and KLF2 Cross-Talk in Shear Mediated Intimal Hyperplasia

Smoking causes blood vessels to constrict or narrow. Tobacco use is a critical risk factor for occlusive artery disease, a leading cause of death in the U.S. Tobacco use accounts for seventy-five percent of all cases of peripheral vascular disease, with smokers having 16 times greater risk than nonsmokers. Treatment for these vascular diseases often requires surgery to re-open the blood vessels, which is called surgical revascularization. These revascularizations frequently fail due to intimal hyperplasia, which is a substantial increase in the intimal (innermost) cells lining the blood vessel, causing it to re-close. Despite the understanding that intimal hyperplasia contributes to the failure of arterial revascularizations, there are no effective treatment strategies to prevent it. We have previously demonstrated that loss of interleukin 1, a growth factor, significantly reduces intimal hyperplasia in mice. Tobacco smokers exhibit amplified levels of interleukin-1, which can act cooperatively with tobacco to increase inflammation. The studies in this grant are targeted to further understand the mechanism by which interleukin-1 mediates intimal hyperplasia both independently and with other molecules, which is of particular interest to tobacco smokers given their higher incidence of vascular disease, higher revascularization failure, as well as their increased levels of interleukin-1. Our objective is to develop therapies to reduce intimal hyperplasia following vascular interventions in order to improve outcomes from these surgeries.

Palta, Jatinder
2009 RC1
University of Florida
$740,838

Ensuring Quality Care for Radiation Therapy Patients

The purpose of this grant is to develop a system that is designed to store each cancer patient's life-long medical records. The system will store medical history, medical care records, medications, lab reports, diagnostic images, radiation therapy data, health monitoring data, and adverse reaction profile. In a typical scenario, these records are often scattered around different healthcare facilities. There is a dire need to provide an electronic health record system for cancer patients, especially those who will receive radiation (two-thirds of newly diagnosed cancer patients). Radiation therapy balances the probability of inducing a curative effect on tumor-laden tissues against the probability of inducing possibly debilitating or catastrophic adverse side-effects in the patient. Therefore, immediate access to a cancer patient's lifelong medical records is extremely important. With our system, this capability will be made available on demand to the radiation oncology community via secure World Wide Web technology. Web-based access to a radiation therapy patient's medical records will mitigate existing geographical and temporal constraints. With internet access and proper security privileges, healthcare providers will be able to access the data from any location and review it in an interactive and collaborative manner. Furthermore, a Web-based electronic peer review system will dramatically improve the safety and quality of care for radiation therapy patients.

Pennypacker, Keith
2009 TSP
University of South Florida
$764,174

Synthesis and Screening of Sigma Ligands for Stroke Treatment at Delayed Time Points

Every year over 800,000 Americans suffer a stroke, and 170,000 of these individuals will die as a consequence of this disease. One of the most significant consequences of cigarette smoking is a pronounced increase in the risk for ischemic stroke. Currently, the only FDA-approved treatment for stroke has a narrow, three-hour window for use and has potentially hazardous side effects. Only 1-2 percent of all stroke patients are currently candidates for this treatment, and thus, there is a great need to discover new drugs for this disease. Finding new effective therapies to treat stroke will save not only many patients' lives but also will likely enhance the quality of life for these individuals by decreasing the severity of physical disability caused by the stroke. We have recently discovered that the compound, 1,3-di-o-tolylguanidine (DTG) can be safely administered to rats after experimental stroke. This compound reduces the damage to the brain caused by stroke injury by at least 80 percent and opens the window of treatment to at least 24 hours, an eight-fold increase over the current available therapy. The goal of this grant is to develop new drugs based on the structure of DTG to improve stroke treatment further by expanding the therapeutic window and decreasing the likelihood of adverse side effects.

Pledger, W. Jackson
2009 TSP
H. Lee Moffitt Cancer Center & Research Institute
$1,000,000

Regulation of Lung Cancer Growth by Postranslational Protein Modifications

The spectrum of diseases linked to tobacco use are not restricted to former smokers, but extend to those exposed to environmental tobacco smoke, making it one of this country's top health priorities. Part of the difficulty in dealing with these diseases is the complexity of the lung environment, which includes epithelial cells that become neoplastic (displaying abnormal, uncontrolled growth) and cells of the immune system that cause airway inflammatory disease. The development of these diseases is not dependent on a single cell type, but rather on changes that may occur in one cell type that are then complemented or amplified by other cells in the local environment or the immune system to cause clinically apparent disease. Studies of cell-cell communication are in their infancy, and approaches able to address this issue hold great promise in the development of useful therapies. In the case of airway disease, a class of compounds that inhibit histone deacetylase (HDAC) enzymes provides a promising therapy for both COPD (chronic obstructive pulmonary disease) and lung cancer. This grant seeks to understand how protein modification regulates cell growth, survival, and inflammatory function as they relate to cell types involved in lung disease. It is the long-term goal of this project to use the resulting knowledge to understand how tobacco use affects tumor initiation, progression, escape from immune surveillance, and therapeutic resistance in lung cancer.

Podack, Eckhard
2009 TTCP
University of Miami
$100,000

Novel Treatment Modality for Asthma

Tobacco smoke is directly responsible for chronic lung inflammation and asthma and aggravates pre-existing allergic reaction predisposing to asthma. Asthma is a chronic, progressive disease for which there is no cure, although treatment to alleviate symptoms is available in most but not all cases. Asthma is a major and increasing health problem in about 7 percent of the American population causing enormous suffering and health-related expenses. In our model studies of lung inflammation and asthma in mice, we have identified the earliest step in the chain of events leading to allergic lung inflammation and asthma, which is associated with excessive mucus production and difficulty of breathing. We also have identified an antibody that can completely block allergic lung inflammation and asthma even when given at a time when inflammation has already initiated. Since the antibody is interrupting the very early steps in the disease process, it has great promise as an effective treatment of asthma. In this grant, the mouse model for asthma will be further studied to determine whether the antibody can also reverse anatomical changes in the lung that occur in chronic asthmatic patients. In addition, the antibody will be engineered by DNA technology to develop a novel treatment modality for patients. The construction of humanized antibodies for the treatment of asthma is the first step in the design of clinical trials, which will be carried out in the following years.

Rai, Priyamvada
2009 NIR
University of Miami
$375,000

Exploring a Role for Oxidative Stress and Oxidative DNA Damage in Limiting the Progression of Non-Small Cell Lung Carcinomas (NSCLCs)

Exposure to tobacco smoke is the leading cause of non-small cell lung carcinoma (NSCLC), a commonly occurring malignant and chemotherapy-resistant form of lung cancer. Many NSCLC's express mutated forms of a protein called Ras that predisposes cells to becoming cancerous. Mutant Ras expression leads to increased cellular reactive oxygen species (ROS) and DNA damage, stresses that usually kill cells or prevent their proliferation. Yet NSCLC cells are able to tolerate Ras despite having impaired processes for repairing oxidative DNA damage. We hypothesize that NSCLCs require compensatory protective processes in order to avoid these cell-toxic and tumor-suppressive effects. It has been reported that NSCLC tumors have elevated levels of an enzyme, human MutT homolog1 (MTH1), which detoxifies oxidant-damaged building blocks of DNA, thus reducing the need for DNA repair. Our preliminary results show that reduction of MTH1 protein protect cells from Ras-induced oxidative DNA damage and that reduction of MTH1 levels in an NSCLC-derived human cell line impairs its tumor formation ability in mice. Thus, using cellular and mouse NSCLC models, the objective of our grant is to assess if inhibiting MTH1 expression limits tumor growth and can sensitize NSCLC cells to certain forms of chemotherapy. Our studies are likely to provide information for the development of novel chemotherapeutic regimens via use of pharmacological MTH1 inhibitors to halt NSCLC tumor progression.

Rodrigues, Claudia
2009 NIR
University of Miami
$375,000

Mechanisms of Intercellular Communication During Angiogenesis

Cardiovascular disease (CVD) is the leading cause of death in the United States. Smokers have twice the risk of heart attack as nonsmokers, and one-fifth of the annual 1,000,000 deaths from CVD are attributable to smoking. Chemicals present in tobacco smoke damage the heart and blood vessels, compromising their function and worsening clinical symptoms. Current treatment of damaged blood vessels consists of surgical restoration of blood flow to compromised tissues. Therapeutic angiogenesis is a new treatment that consists of induction of new blood vessel growth and might help patients who cannot benefit from current treatments. Understanding how blood vessels are formed is critical for the development of therapeutic angiogenesis. Blood vessel formation involves the interaction of different cell types. Progenitor cells have the potential to become different cell types like endothelial cells (ECs), smooth muscle cells (SMCs) or pericytes. ECs form the inner layer of all blood vessels, while SMCs and pericytes are located on the outer side and control blood vessel permeability. Progenitor cells are recruited to sites of new blood vessel growth where signals from this microenvironment trigger their transformation into new ECs, SMCs, and/or pericytes. We have recently shown that the protein c-Myc is required for blood vessel growth. Our goal is to understand the mechanisms by which c-Myc regulates this process. We will specifically determine the requirement of c-Myc for progenitor cell attachment to endothelial cells and the molecular mechanisms involved.

Rose, Dorian
2009 NIR
University of Florida
$375,000

Use of Repetitive Transcranial Magnetic Stimulation as an Adjuvant to Enhance Post-Stroke Recovery

Tobacco use has long been identified as an independent risk factor for stroke. Up to 25 percent of all strokes are directly attributable to cigarette smoking, which independently increases the relative risk of stroke three-fold. Loss of movement and associated loss of function, decline in societal participation, and depression make stroke one of the most devastating tobacco-related health conditions. Stroke is the leading cause of long-term disability in this country with more than 1 million Americans reporting difficulty with daily activities. With stroke primarily striking those over 65, these sequelae are especially manifest in Florida. Loss of independence in self-care tasks is primarily due to limited recovery of the arm. The long-term goal of this study is to develop rehabilitation programs that restore movement and function of the arm post-stroke. In this grant, we will determine if the addition of low-frequency Transcranial Magnetic Stimulation (TMS) to inhibit the overactive contralesional hemisphere (side of the brain opposite the stroke), to progressive functional task exercise of the weakened arm will improve arm recovery to a greater degree than arm exercise alone. Individuals who are post-stroke secondary to tobacco use will participate in 16 sessions of 1) arm rehabilitation alone or 2) arm rehabilitation plus TMS. We will assess arm movement ability and function immediately following the 4-week intervention and at a 30-day follow-up to determine retention of immediate gains.

Ross, Owen
2009 NIR
Mayo Clinic
$375,000

Investigation of the Familial CADASIL Gene NOTCH3 in Ischemic Stroke

Fifteen million people worldwide suffer a stroke each year with devastating effects; one-third of these individuals die and another one-third remain permanently disabled. Lessons from other neurodegenerative disorders have shown that genetic causes of familial forms of disease may influence sporadic manifestation. This study will explore the relationship between variation at the NOTCH3 locus (a familial stroke gene mutation) and susceptibility to ischemic stroke. We have DNA available for 200 well-characterized familial ischemic stroke patients, 1786 individuals who have suffered sporadic ischemic stroke, and 2000 ethnically matched control individuals. We have detailed clinical phenotypic information including tobacco-related habits, diabetes, hypertension, and obesity in our stroke patients. Establishing the joint effects of NOTCH3 genetics and environmental factors has the potential to identify subsets of at-risk individuals and to help with preventative diagnosis and treatment. Functional resolution of genetic variants influencing stroke susceptibility will provide insights into the pathology of stroke and may also be the driving force behind the generation of both in vitro and in vivo model systems, which will allow safety and efficacy profiling in the development of targeted therapeutics.

Salathe, Matthias
2009 SIG
University of Miami
$204,902

Computer-Controlled Tobacco Smoke Delivery System for Cell Cultures

The instrument provided through this grant is a Vitrocell Cultivation and Exposure System for Tobacco Smoke. The equipment is a robot that will deliver mainstream tobacco smoke as well as side stream or environmental tobacco smoke to normal human bronchial epithelial cells cultured at the air-liquid interface, effectively mimicking the tobacco smoke exposure of human airways in smokers in real life. The bronchial cells are cultured in a two-chamber system allowing nutrient medium to be applied to the bottom of a porous support under the cells, while the top is exposed to air in the same way as cells in the bronchus. This equipment controls puff volume, duration, and frequency of smoke delivered to each culture in multi-well plate formats. This instrument is essential to study the effects of smoking on airway epithelia accurately. Other approaches to studying smoking effects do not accurately reproduce smoke exposure. For example, some studies have used an aqueous extract of tobacco smoke prepared by bubbling the smoke through saline solution. Such extracts lack the gaseous components and permit changes in the smoke components before the extract can be applied to cells. Furthermore, in real life, the cells are only exposed to the smoke, not to liquid on the air surface of the cells. Thus, this smoke exposure robot provides new capabilities that are not currently available to these projects.

Schabath, Matthew
2009 NIR
H. Lee Moffitt Cancer Center & Research Institute
$375,000

Molecular Epidemiology of Lung Cancer Survival: A Pathway Approach

Globally, lung cancer is the most common tobacco-related disease. Despite the current knowledge about the deadly and deleterious effects of cigarette smoking, the prevalence of smoking in the U.S. has not seen drastic declines over the last decade. More people die from lung cancer than any other type of cancer in the U.S., and lung cancer accounts for more deaths than breast cancer, prostate cancer, and colon cancer combined. Over the last 40 years, lung cancer survival has not improved significantly, and the 5-year survival rate for all stages combined remains a dismal 15 percent. Hence, there is an immediate need to develop lung cancer survivorship studies to investigate genetic and environmental factors and their influence on lung cancer survival. The objective of this grant is to analyze genetic factors and environmental exposures for lung cancer survivorship using data from a cohort of lung cancer patients. The long-term objectives of this research are to improve lung cancer survival and to develop multidisciplinary lung cancer studies in collaboration with clinicians, basic scientists, geneticists, and biostatisticians. This research has tremendous societal implications by identifying high-risk individuals for poor survival and prognosis and provides an approach for individualized treatment based on genetic and environmental exposure profiles.

Tockman, Melvyn
2009 TTCP
H. Lee Moffitt Cancer Center & Research Institute
$100,000

Centrosome Measurement in Diagnosis and Prognosis of Lung Cancer; Validation and Optimization

Centrosomes organize chromosomes in the nucleus of a cell. Loss of centrosome integrity causes chromosomal instability in lung cancer. In our previous work with lung cancer cells, we identified the pathway of centrosome breakdown as well as how to alter that pathway and thus stabilize centrosome number, structure, and reduce lung cancer cell proliferation. Our novel centrosome image algorithm recognizes these changes and discriminates normal from cancer cells in culture and in a small number of histology specimens. Centrosome image analysis suggests that centrosome instability is an important target in lung cancer, a marker of abnormal and uncontrolled cell growth, a potential cellular dosimeter of chromosomal instability, and may allow individual prediction of cancer treatment response. In Aims 1 and 2, we plan to examine our earlier tissue culture observations in a case-control study of 160 lung cancer and adjacent uninvolved tissue specimens resected from patients treated and followed at Moffitt. We will determine whether quantitative centrosome assessment of an individual's lung cancer, adjusting for clinical information, identifies the cancer, and predicts treatment response and patient survival. In Aim 3, we partner with IntelliSense Design, Inc., who specializes in control software and pattern recognition, to automate image acquisition and analysis, enhancing instrument design and commercialization, to develop data for an STTR application to build and validate an instrument.

Verdun, Ramiro
2009 NIR
University of Miami
$375,000

DNA Damage Proteins and Telomerase Activity in Tumor Cells

Telomeres are specialized structures found at the extreme ends of chromosomes that preserve genomic stability and maintain cell-proliferative capacity. Telomeric shortening occurs in most human cells as an inevitable consequence of normal cell division. Critical shortening of telomeres produces dysfunctional telomeres that are recognized as damaged and thus halt cell division. In cancer cells, telomere loss can be counteracted by the activity of an enzyme called telomerase, which elongates the telomeres and thus confers to the cells an "immortal" state. This process is illustrated by the finding of recent reports showing that telomerase activity is essential for both small and non-small cell lung cancer cell formation and maintenance. We know that the telomere elongation by telomerase is restricted to cells that are dividing. However, we don't know at what moment of the cell division telomerase is recruited at the telomeres or which proteins could be controlling its activity. This research aims to study how and when the telomerase is loaded to the chromosome ends. For this purpose, we will use molecular and cellular biology techniques that will reveal when and which proteins are located at the telomeres when the telomerase is elongating our chromosome ends. From these studies, we expect to arrive at a molecular model that reveals how tumor cells maintain their telomeres.

Wanner, Adam
2009 RC1
University of Miami
$748,400

The Airway Microbiome in COPD

The air passages are exposed to a variety of environmental factors including microorganisms. In healthy persons, the host defenses of the lung clear the microorganisms thereby preventing them from causing an inflammatory response that can damage the airways. It is known that cigarette smoke impairs the host defense system allowing colonization of the airways with microorganisms, and this could be one mechanism whereby cigarette smoke causes COPD. In this study, we are testing the hypothesis that the types of microorganisms harbored by the lung are different in smokers and non-smokers, and also different in smokers with and smokers without COPD. We will do this by obtaining secretions from the lung by bronchoscopy (an instrument that allows the operator to view the airways), determining the spectrum of microorganisms in them using a modern gene-based technology, and relating the microbial findings to the presence or absence of clinical COPD in smokers. Should such a relationship emerge in the study, therapeutic agents directed at selected microorganisms could be developed as a novel treatment for COPD.

Wu, Jang-Yen
2009 RC1
Florida Atlantic University
$748,046

G-CSF, DETC-MeSO and Sulindac as Multi-drug Combination Therapy for TBI and Stroke Treatment

It is known that cigarette smoke greatly increases the risk of stroke, and stroke-induced brain injury is largely due to excessive glutamate excitation known as excitotoxicity. No effective therapeutic intervention for stroke has been developed yet. Recently we have shown that granulocyte colony-stimulating factor (G-CSF), an FDA approved drug, is effective in restoring the brain function in Parkinson's disease and stroke. In addition, we also found two additional drugs, DETC-MeSO and sulindac, which protect the brain via different mechanisms. DETC-MeSO is a glutamate receptor partial antagonist and is an active metabolite of disulfiram, a widely used drug for treatment of alcoholism. Sulindac is also an FDA-approved drug as an anti-inflammatory agent, and is a catalytic antioxidant. Based on these findings, we propose to use a three-pronged approach by combining G-CSF, a stem cell enhancer and facilitator; DETC-MeSO, a glutamate receptor partial antagonist; and sulindac, a potent antioxidant, representing three different classes of drugs as a multi-drug combination therapy for stroke. Information obtained from the proposed studies may provide an effective and novel multi-drug treatment for stroke.

Zhang, Xiaohong (Mary)
2009 NIR
University of South Florida
$375,000

Mechanisms by which HDAC6 Confers Chemoresistance in Lung Cancer

With 1.2 million new cases diagnosed every year, lung cancer is the leading cause of cancer-related mortality in both men and women. Two first line regimens of lung cancer treatment are platinum with taxane and platinum with gemcitabine. One of the major obstacles of these treatments is that patients often develop resistance to platinum. Histone deacetylases (HDACs), are enzymes involved in a wide variety of biological processes including transcription regulation, cell growth/differentiation, cell death, etc., and are thought to play a role in developing platinum resistance. HDAC inhibitors now hold great promise in cancer treatment in that they could restore the chemo-sensitivity in tumor cells, including lung cancer cells. However, the role of these enzymes in chemo-resistance is largely unknown. Our preliminary data show that one of the HDACs, termed HDAC6, interacts with and modifies the DNA mismatch proteins, which play critical roles in the recognition of DNA-cisplatin complex and trigger programmed cell death. Cisplatin is one of the most widely used platinum compounds in lung cancer treatment, and we will use it as a representative drug to study platinum-resistance. Therefore, in this grant, we will investigate the mechanisms by which HDAC6 confers cisplatin-resistance via modification of DNA mismatch repair proteins in lung cancer. The results of our research will identify HDAC6 as a novel therapeutic target in lung cancer and suggest the application of clinically relevant HDAC6-selective inhibitors as agents to enhance the efficacy of chemotherapy drugs.

Zhou, Ming-Sheng
2009 NIR
University of Miami
$375,000

Mechanisms Underlying Nicotine's Proatherogenic Effects in Macrophages

Cigarette smoking is a significant risk factor for development of cardiovascular diseases. Cigarette smoking is known to contain various components that are distributed in both particulate and gaseous phases. One of the major active components of cigarette smoking is nicotine. Nicotine has been shown to contribute to many of the toxicities related to cigarette smoking, and has also been shown to promote atherosclerosis. Atherosclerosis is considered to be a chronic vascular inflammatory disease associated with excessive lipid (cholesterol) accumulation in the vascular wall. Macrophages (one type of white blood cells) play an important role in the progression of atherogenesis through the accumulation of cholesterol and the production of inflammatory cytokines (cellular factors). We have recently identified that human macrophage nicotine increases the expression of CD36, an important intracellular signaling molecule in the regulation of lipid metabolism and inflammatory factors expression. The long-term goal of this study is to clarify the molecular mechanisms by which nicotine contributes, promotes, or accelerates atherosclerotic cardiovascular disease. In this grant, we will investigate how nicotine increases CD36 expression (intracellular signaling pathway) in macrophages and how increased CD36 contributes to atherogenic effect of nicotine. The findings from this grant will provide valuable information to develop new strategies for the prevention and treatment of smoking-related cardiovascular diseases.

Appendix E.
National Institutes of Health, Funding by State

2009-2010 Funding by State[22]

Listed below are the 30 states that received the most NIH funds.

State	2008 Population Estimate	Pop Rank	$ Per Capita	Per Capita Rank	Funding 2009	Rank	% of Total Funding
California	36,756,666	1	104.81	11	3 ,852,635,114	1	14.97%
Massachusetts	6,497,967	15	436.09	1	2 ,833,691,479	2	11.01%
New York	19,490,297	3	118.97	9	2 ,318,843,227	3	9.01%
Pennsylvania	12,448,279	6	133.27	7	1 ,658,949,181	4	6.45%
Texas	24,326,974	2	52.77	29	1 ,283,792,023	5	4.99%
Maryland	5,633,597	19	209.66	3	1 ,181,164,081	6	4.59%
North Carolina	9,222,414	10	123.74	8	1 ,141,200,696	7	4.44%
Washington	6,549,224	13	145.62	6	9 53,722,128	8	3.71%
Illinois	12,901,563	5	68.54	21	8 84,249,726	9	3.44%
Ohio	11,485,910	7	66.94	22	7 68,868,347	10	2.99%
Michigan	10,003,422	8	72.32	20	723,445,320	11	2.81%
Missouri	5,911,605	18	95.86	13	5 66,692,757	12	2.20%
Connecticut	3,501,252	29	155.98	5	5 46,123,975	13	2.12%
Tennessee	6,214,888	17	87.69	15	5 44,989,237	14	2.12%
Minnesota	5,220,393	21	97.82	12	5 10,674,925	15	1.98%
Georgia	9,685,744	9	52.06	30	5 04,282,942	16	1.96%
Florida	**18,328,340**	**4**	**25.40**	**42**	**465,523,665**	**17**	**1.81%**
Wisconsin	5,627,967	20	78.28	17	4 40,557,695	18	1.71%
Virginia	7,769,089	12	48.95	32	3 80,289,061	19	1.48%
Colorado	4,939,456	22	75.88	19	3 74,812,302	20	1.46%
Oregon	3,790,060	27	88.75	14	3 36,385,033	21	1.31%
New Jersey	8,682,661	11	34.17	39	2 96,650,313	22	1.15%
Alabama	4,661,900	23	62.25	26	2 90,204,124	23	1.13%
Indiana	6,376,792	16	40.72	37	2 59,636,393	24	1.01%
Iowa	3,002,555	30	76.68	18	2 30,235,893	25	0.89%
District of Columbia	591,833	50	378.50	2	2 24,006,642	26	0.87%
Arizona	6,500,180	14	29.39	40	1 91,049,310	27	0.74%
Kentucky	4,269,245	26	44.47	34	1 89,844,749	28	0.74%
South Carolina	4,479,800	24	41.03	36	1 83,791,285	29	0.71%
Rhode Island	1,050,788	43	167.90	4	1 76,431,861	30	0.69%
Utah	2,736,424	34	64.44	25	1 76,337,072	31	0.69%
Louisiana	4,410,796	25	34.43	38	1 51,880,069	32	0.59%
New Mexico	1,984,356	36	66.36	23	1 31,684,305	33	0.51%
Kansas	2,802,134	33	41.42	35	1 16,056,445	34	0.45%
New Hampshire	1,315,809	41	86.45	16	1 13,754,229	35	0.44%
Nebraska	1,783,432	38	60.96	27	1 08,719,358	36	0.42%
Maine	1,316,456	40	64.78	24	8 5,286,230	37	0.33%
Arkansas	2,855,390	32	27.46	41	7 8,398,266	38	0.30%
Vermont	621,270	49	118.57	10	7 3,661,223	39	0.29%
Hawaii	1,288,198	42	52.99	28	6 8,267,754	40	0.27%
Oklahoma	3,642,361	28	17.58	48	6 4,021,647	41	0.25%
Montana	967,440	44	49.70	31	4 8,084,727	42	0.19%
Delaware	873,092	45	44.86	33	3 9,162,645	43	0.15%
West Virginia	1,814,468	37	17.77	47	3 2,240,354	44	0.13%
Mississippi	2,938,618	31	10.91	49	3 2,068,251	45	0.12%
Nevada	2,600,167	35	9.43	51	2 4,531,519	46	0.10%
South Dakota	804,194	46	23.56	44	1 8,949,612	47	0.07%
Alaska	686,293	47	23.73	43	1 6,285,062	48	0.06%
North Dakota	641,481	48	23.42	45	1 5,024,898	49	0.06%
Idaho	1,523,816	39	9.70	50	1 4,782,993	50	0.06%
Wyoming	532,668	51	18.08	46	9 ,632,407	51	0.04%
Total	**304,059,724**		**80.02**		**25,731,572,550**		**100.00%**

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