JAMES & ESTHER KING BIOMEDICAL RESEARCH PROGRAM

2006 Annual Report

January — December 2006

Building a Portfolio

February 1, 2007

The Honorable Charlie Crist, Governor
The Honorable Ken Pruitt, Senate President
The Honorable Marco Rubio, House Speaker
Secretary Ana M. Viamonte Ros, M.D., M.P.H., Florida Department of Health

Dear Governor Crist, President Pruitt, Speaker Rubio, and Secretary Viamonte Ros:

On behalf of the entire Biomedical Research Advisory Council, I am pleased to present the 2006 James and Esther King Biomedical Research Program Annual Report, pursuant to section 215.5602, *Florida Statutes* summarizing the overall status of the program and its accomplishments to date.

Florida's investment in this program is yielding a number of important benefits. Sponsored investigators across the state are producing important scientific findings leading to better prevention, diagnosis, treatment, and cure of tobacco-related diseases plaguing Floridians. Many awardees are leveraging King Program awards to earn additional funding from external sources. Some of their discoveries are leading to new start-up companies with significant commercial potential. In support of our state's biotechnology initiatives, this program is helping to build the biomedical research capacity of the state by attracting and retaining highly qualified and productive biomedical researchers at all experience levels at our Florida institutions.

Obtaining funding from the National Institutes of Health and other federal agencies with biomedical interests has become markedly more difficult since 2003, and this trend is unlikely to be reversed in the near future. The James and Esther King Biomedical Research Program, along with other grant programs sponsored by the state of Florida, such as the Bankhead-Coley Cancer Research Program, gives Florida an advantage over other states (and in some cases, other countries) by offering talented scientists and clinical researchers more opportunities to access resources needed to conduct break-through research. By conducting state-wide open competitions and consulting unbiased national experts in project selection, the state is assured that funded projects represent top quality research with the greatest potential to improve human health.

We are grateful for the confidence expressed by the governor's office and the state legislature in this program during its 2006 reauthorization, and we accept the challenge to invest and manage program funds fairly and wisely. Our fellow citizens deserve a model biomedical research program, and perhaps more importantly, a greater likelihood of success in preventing and treating tobacco-related diseases such as cancer, cardiovascular disease, stroke, and pulmonary disease.

I invite you to familiarize yourselves with the 2006 accomplishments, business processes, and fiscal management described in this report, and ask for your vigorous support as we continue our efforts to maximize the results delivered by the James and Esther King Biomedical Research Program.

Sincerely,

Dr. Richard J. Bookman

Chair, Florida Biomedical Research Advisory Council

This 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.

James and Esther King Biomedical Research Program

Annual Report
January–December 2006

Submitted to

The Governor
The President of the Senate
The Speaker of the House of Representatives
The Secretary of the Department of Health
State of Florida

and

The Florida Center for Universal Research to Eradicate Disease

by

Biomedical Research Advisory Council
Dr. Richard Bookman, Chair

February 1, 2007

Executive Summary

Since the initial grants awarded in 2001, the James and Esther King Biomedical Research Program has transformed the investment of more than $45 million from the state of Florida over the last six years into a diverse portfolio of productive research toward preventing, diagnosing, treating, and curing tobacco-related disease.

Conducted by scientists and clinicians throughout the state, these projects represent basic science, applied research, and clinical application. Some of the research addresses behavioral issues or crosscutting science, while other disease-specific studies target cancer, cardiovascular disease, stroke, and pulmonary disease. A number of projects also hold promise for boosting the biotechnology sector of the Florida economy.

The program is building the state's biomedical research capacity by providing support for investigators at all experience levels, with particular emphasis given to encouraging new investigators to launch successful independent research careers at institutions in Florida. During 2006, 49 Florida researchers led program-sponsored research, and these funded projects provided significant financial support and research experience for 65 predoctoral or postdoctoral students. Principal investigators demonstrated their productivity with 81 presentations and 36 articles published in peer-reviewed journals in 2006, and leveraged program grants to earn awards totaling more than $10 million in external funding during the year.

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In February 2006, researchers submitted 51 applications for program funding, collectively seeking more than $20 million. The Florida Biomedical Research Advisory Council considered the results of a rigorous national peer review process in making new funding recommendations, and as a result, the program launched 17 new projects on July 1.

The National Institutes of Health (NIH), awarded $331 million to Florida researchers in fiscal year (FY) 2006, $36 million less than in the prior year. As federal funding is becoming increasingly difficult to obtain, this program is filling an important funding gap for the state's research community.

It was a year of great change within the advisory council, as the terms of six of its nine members expired, and new legislation expanded its membership to eleven. With one vacancy remaining at year-end, seven new appointees stepped up to the challenge of continuing the work of their predecessors in maintaining momentum in this program, along with starting up the new Bankhead-Coley Cancer Research Program.[1]

Program staff audited 12 grants during site visits in 2006, gathered comprehensive information about research progress, and solicited feedback for consideration in making program improvements. Twenty-five multi-year awards made in prior years were renewed for another year of funding after demonstrating satisfactory progress against specific research milestones. Lack of progress led program staff to discontinue one grant and suspend payment on another pending evidence of further scientific progress.

In December, the program released a call for grant applications for FY 2007-2008, setting in motion the process of putting another cadre of Florida researchers to work in the fight against tobacco-related disease.

With the passage of House Bill 1027 in 2006, the Florida Legislature continued funding through 2010, at which time lawmakers will comprehensively assess the performance of the program against the goals and intent of the state's investment.

The objectives for the following pages are to illustrate clearly the depth and breadth of the portfolio of promising research currently underway, to describe plainly how the Office of Public Health Research manages the program, and to relay convincingly that all associated with the program are firmly committed to deliver on this opportunity.

Program Vision and Goals

The addictive power of nicotine and the consequential exposure to tobacco smoke continues to keep many Floridians in the grips of a host of tobacco-related diseases. It has been over forty years since the publication of the first Surgeon General Report linking smoking to cancer, yet tobacco use remains the leading cause of preventable mortality in the United States. Nearly 22 percent of Floridians smoke cigarettes[2] – a number that has remained relatively constant over the last ten years. As a result, tobacco-related diseases in Florida continue to represent a significant burden for our state's healthcare delivery systems; more importantly, they take a physical, emotional, and economic toll on our families and friends. To address this challenge the Florida Legislature continues to support the James and Esther King Biomedical Research Program in order to target specific research towards prevention, diagnosis, treatment, and cure of diseases related to tobacco use.

"In 2004, 12,360 Floridians died of lung cancer. However, with each new investigator helped by the James and Esther King Biomedical Research Program, Florida residents will continue to benefit from leading edge, life-enhancing treatments unavailable to previous generations. It's simply one of the most compassionate ways we can care for our citizens while continuing to broaden the scope of current scientific knowledge."

— Dr. William Self
University of Central Florida
2005 New Investigator Research Grant

As defined in Florida law,[3] the 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

As the means for achieving these goals, the state charges the program with awarding grants and fellowships to qualified investigators throughout the state based on scientific merit as determined by an open, competitive peer review process.

With consultation from the Biomedical Research Advisory Council, the program has concentrated in the near term on investing the available funds to build a diverse portfolio of research projects as a foundation for future progress. Program-funded research targets a wide range of tobacco-related diseases, spans the spectrum of science from basic research to clinical application, and offers opportunities for qualified investigators working across the state.

Program Impact

Unfortunately, there are no quick solutions to eradicate diseases stemming from, related to, or exacerbated by the use of tobacco. However, over the course of the last 12 months there is much to show for Florida's investment in the James and Esther King Biomedical Research Program. Project investigators documented their discoveries in articles published in major scientific journals and attracted national funding. The program launched a new cluster of promising research projects. The cadre of multi-disciplined scientists and community practitioners in the state grew stronger as program support helped talented new investigators find a productive home in the Florida research community and made new projects possible for some of the best of those already here. Fledgling businesses emerged to begin taking promising new developments to a wide market. All are contributing to systematically build knowledge and introduce new approaches that are leading to new successes in preventing, diagnosing, treating, and ultimately curing cardiovascular disease, stroke, pulmonary disease, and cancer.

> "The Small Business Technology Transfer Grant allowed us to further develop [nanomagnetic particle] technology which has resulted in our fourth patent."
>
> — Dr. Ching-Jen Chen
> Florida State University
> 2005 Small Business Technology Transfer Grant

Each of the following sections presents a different perspective on the program's growing research portfolio and illustrates the significant progress made possible with the investment of program grants.

"The James and Esther King Biomedical Research Program is a tremendous resource for new investigators working in the state of Florida. This program provides a great funding opportunity as well as encouraging mentorship throughout the entire funding period. Funding from the James and Esther King Biomedical Research Program has prepared me for the recent submission of my first independent research grant proposal, an R01, to the National Institutes of Health."

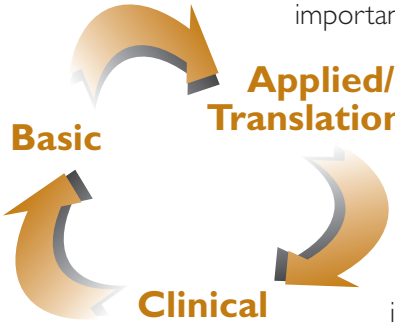
— Dr. Erin Siegel
H. Lee Moffitt Cancer Center & Research Institute
2005 New Investigator Research Grant

Dr. Erin Siegel (center), Dr. Anna Guiliano — Mentor (right), Dr. Tom Sellers — Co-Mentor (left).

Investment and Progress

Working Bench-to-Bedside and Back

A key factor in the program's success is ensuring that the portfolio of research includes studies along the continuum of basic, translational, and clinical areas. A bench-to-bedside balance in research begins with studies designed to improve our understanding of molecular or cellular level functions. Discoveries and results from basic research often lead to useful intermediate applications (applied or translational research) that enable progress towards research at the clinical level; successes in clinical research ultimately lead to new treatments ranging from drugs and vaccines to radiotherapy solutions and beyond. It is important to recognize that the bench-to-bedside approach is bidirectional, as findings in the field can raise questions that pinpoint a need for better understanding of the basic science underlying the phenomenon. Successful discoveries depend on a steady stream of research and data flowing between basic and clinical studies to accomplish results.



Although everyone benefits when discoveries become effective treatments, no one wants a treatment that has not been tested properly for safety and efficacy. The journey from the lab to application may span many years and proper evaluation may involve lengthy protocol development and testing before, during, and after clinical trials. Patients must be recruited, enrolled, and screened. Data must be collected, analyzed, published, reviewed, and replicated. This process of discovery, application, and translation takes time (sometimes decades) and roadblocks or unexpected outcomes often cause a return to the bench to understand results or try new approaches.

The James and Esther King Biomedical Research Program's ongoing support of research at all stages is significant to balancing a research portfolio that is likely to result in successful outcomes. In looking at the research projects funded since 2001, approximately one quarter of the studies have been clinically oriented, with the balance split nearly evenly between basic science and applied/translational studies (Figure 1). Approximately one-third of the translational projects funded to date have supported projects involving human cells or human tissue; the other two-thirds carry basic science forward by means such as using animal models to predict the potential effect in humans or by developing medical devices.

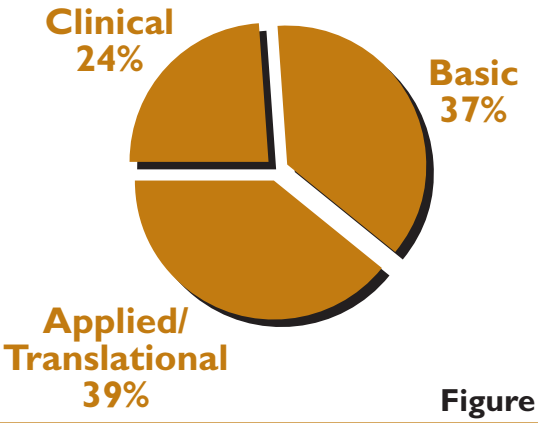


Figure 1
Stage of research projects funded to date

Grantee Profile

Glen Barber, Ph.D.

University of Miami, 2004 Team Science Program Grant
Principal Investigators: Beatriz Fontoura, Ph.D., Kerry Burnstein, Ph.D.

A new technique called virotherapy aims to combat cancer by harnessing the insidious nature of the virus. Researchers are testing modified viruses that act as guided missiles, selectively infecting and eradicating tumor cells. A research team led by Dr. Glen Barber at the University of Miami is using their James and Esther King Biomedical Research Program Team Science Program grant to determine the effectiveness of the vesicular stomatitis virus (VSV) in targeting tumor growths. VSV is a particularly useful virus because it infects and kills tumor cells rather than healthy cells. Normal cells are able to protect themselves by creating specific proteins called interferons that inhibit VSV replication. However, due to the irregularities present in cancer cells, VSV is able to invade, replicate, and either break tumor cells apart or sufficiently weaken them, making them more susceptible to traditional chemotherapies. Another major part of virotherapy's appeal is its efficiency. During treatment, not all cancerous cells need to be infected at once because the virus will naturally spread and hunt out cancerous cells, increasing its killing effect.

Dr. Barber's team has been especially encouraged by the versatility of VSV. "VSV will bind to nearly every cell type, so the challenge is to modify it in such a way that it will select specific cell types. For instance, when breast cancer cells develop, they can over-express a certain protein known as EGFR. However, if we can customize VSV by adding molecules to the virus that bind to EGFR, we can zero in on breast tissue tumors while leaving surrounding tissues perfectly intact." This method may be able to eliminate large amounts of the tumor. Another approach is to include an immunomodulator gene, allowing the viral vector to first to penetrate cancerous cells, and then manufacture the immunomodulatory protein that can enhance an immune response to the tumor at a later stage. One of the viral vectors the team is currently developing includes interferon (VSV-IFN) to stimulate an immune response, which could then eliminate remaining elements of the tumor. This vector also reduces the chance of the virus successfully damaging normal cells. To date, the team has been able to regress cancerous growths in mice substantially by injecting VSV into animals harboring malignant disease.

"Bronchogenic carcinomas, laryngeal and oro-pharyngeal carcinomas, which have a grim prognosis, constitute a considerable percentage of all new cancer diagnoses. Considering that tobacco use is the major cause of premature death in the U.S., new treatment modalities are urgently needed. This type of state funding allows scientists to continually broaden the scope of their research aims," Barber explains. "In working with the King Biomedical Research Program, what stood out most for me was how clearly they understand the nature of scientific inquiry. We were so encouraged by our prior work on breast cancer that this grant meant we could apply that knowledge to a broader spectrum of cancer types. If we can improve treatment modalities and survival rates for head and neck cancers, this bodes extremely well for developing new approaches to other forms of the disease."

The grant also provided part of the funding for the purchase of a high-sensitivity, fluorescence imaging system. "This device has revolutionized our experiments by allowing us to track the location and intensity of the oncoviruses, and non-invasively monitor tumor growth or regression in small rodents."

Investment and Progress

Preventing and Defeating Tobacco-Related Diseases

Medical evidence connecting tobacco usage with a wide range of serious illness led the Florida Supreme Court to rule in July 2006 "that smoking cigarettes causes aortic aneurysm, bladder cancer, cerebrovascular disease, cervical cancer, chronic obstructive pulmonary disease, coronary heart disease, esophageal cancer, kidney cancer, laryngeal cancer, lung cancer (specifically, adenocarcinoma, large cell carcinoma, small cell carcinoma, and squamous cell carcinoma), complications of pregnancy, oral cavity/tongue cancer, pancreatic cancer, peripheral vascular disease, pharyngeal cancer, and stomach cancer." The court also affirmed "that nicotine in cigarettes is addictive."[4] Clearly, the need and the opportunity to contribute to the body of disease-specific knowledge is great.

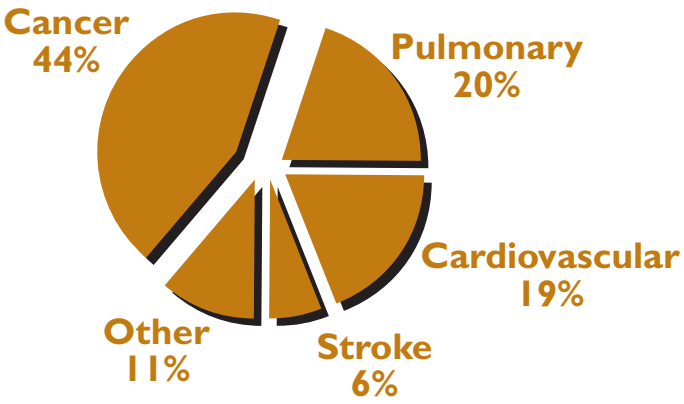


Figure 2

Disease focus of all projects funded to date

Of the 96 research projects funded by the program since 2001, 44 are related to cancer in its many forms. Projects targeting pulmonary and cardiovascular disease have been nearly equally represented, followed in number by research projects involving stroke. The balance has been non-disease specific, and includes work addressing developmental or behavioral research, including the prevention or cessation of smoking (Figure 2).

An examination of the types of grants funded during this period shows that the majority of sponsored researchers are centering their efforts on finding better treatments or cures for smoking-related illnesses (Figure 3). However, a significant share of program funds have also been awarded to support the work of investigators seeking to help prevent the onset of these diseases, and to improve the ability of healthcare providers to better diagnose them when prevention tactics fail.

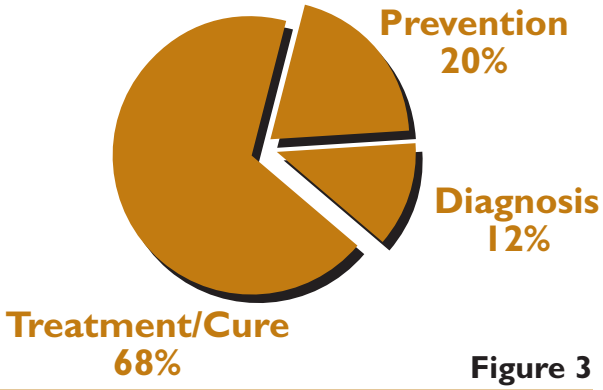


Figure 3

Research goals of all projects funded to date

Appendix A contains a list of all active research projects in 2006, classified by disease focus or basic research emphasis.

Grantee Profile

Mona Boules, Ph.D.

Mayo Clinic, 2004 New Investigator Research Grant

The addictive power of nicotine is well documented. For every successful ex-smoker, many others inevitably relapse. Nicotine addiction is not only a matter of habit and environment, but it can also facilitate biochemical changes in the brain.

Armed with a 2004 New Investigator Research Grant from the James and Esther King Biomedical Research Program, Dr. Mona Boules and her colleagues at the Mayo Clinic in Jacksonville are unlocking the complex neurological basis underlying nicotine's effect on brain chemistry. "We are trying to understand the changes that take place over time to find a way to alter their course. The main goal is to return the brain to its original, pre-addictive state," she explains.

Her team is currently testing a potential new drug, NT69L, which mimics a brain neuromodulator called neurotensin. Neurotensin promotes and/or inhibits the transmission of nerve impulses that Dr. Boules believes is a key factor in nicotine addiction. When nicotine is introduced, dopamine levels are elevated, enhancing mood. However, in the absence of nicotine, smokers will experience the sluggish, depressive feelings common to withdrawal. In developing a "neurotensin analog," or a chemical compound similar in structure to neurotensin, Dr. Boules is able to thwart the craving for nicotine in rats by maintaining a consistent level of dopamine in the brain.

NT69L is also unique in that it can be administered effectively by injection whereas neurotensin, in its original form, must be injected directly into the brain. "We were so excited that the analog was chemically stable and could cross the blood-brain barrier," she explains. "This may allow us to formulate it to be administered in a patch form. Yet, without sufficient funding, we would not have been able to test our hypothesis any further. Our lab didn't have the resources or degree of specialization required to construct the controlled environment needed to test the analog on rats."

The New Investigator Research Grant allowed Dr. Boules' team to purchase and construct an operant conditioning laboratory to test their hypothesis. Initially, rats learned to self-administer food by pressing a lever. Next, they were given the option to self-administer nicotine. When the researchers noticed a heightened level of motor activity indicating nicotine addiction, they administered the neurotensin analog. They soon noticed that the amount of nicotine the rats self-administered per minute dropped by 80 percent.

Not only does the analog diminish nicotine craving, it also shows promise in treating other addictive behaviors by engaging the brain's overall system of "reward pathways." As Dr. Boules explains, "While we're still investigating the exact causes, we know that the neurotensin analog can reduce cravings for other addictive drugs like cocaine and amphetamines. It also counteracts the weight gain associated with nicotine withdrawal because it has an appetite-suppressing effect, which could be due to its interaction with the hormones produced by the hypothalamus, or its modulating effect on the brain's dopamine and serotonin levels."

The analog also displays compatibility with current anti-psychotic medications used to treat schizophrenia. "Patients with mental illnesses, ranging from depression to schizophrenia, have a much higher incidence of nicotine addiction. Schizophrenics in particular have what's known as 'impaired sensory gaiting,' meaning they are unable to prioritize sensory information, causing extreme anxiety and agitation." Studies have shown nicotine temporarily relieves these symptoms by increasing concentration and focus, making it more difficult for these individuals to quit. "Schizophrenics have a much higher success rate when their smoking cessation program coincides with a regimen of anti-psychotic drugs, and this analog is highly biocompatible with those drugs."

Preclinical toxicology studies have begun testing the safety of NT69L, and planning for Phase I clinical trials is already underway. Dr. Boules is currently in the process of filing for a patent and is preparing an application for a grant from the National Institutes of Health. She credits the James and Esther King Biomedical Research Program for opening a whole world of funding that previously seemed unavailable. "An award like this is a major vote of confidence in the eyes of federal funding programs, which are literally buried in applications. It allowed us to demonstrate that we are competent researchers who are able to get results." She has also enjoyed the spirit of collaboration and collegiality that the New Investigator Research Grant helped launch, finding it "incredibly gratifying to cultivate the next generation of scientists who, unlike in previous years, will now stay in Florida after graduation because everything they need to continue their research is right here."

Investment and Progress

Building Research Capacity

The program has placed a high priority on strengthening the state's core research capacity by offering grant mechanisms designed to attract new investigators, to retain scientists and clinicians who have already made the choice to work in Florida, and to help investigators at all experience levels achieve greater success in their research careers. The support provided in building the state's research capacity is evident in another view of the 2006 portfolio of grants:

- Nine multidisciplinary teams of experienced researchers at four Florida institutions received program funding for the conduct of cohesive clusters of projects that established and solidified collaborative research relationships within the state.

- Five partnerships between academic researchers and small businesses in the state jointly pursued the feasibility of moving laboratory research into a commercial market, bringing to nine the total number of such projects supported by the program since 2003.

- For 36 more investigators at eight institutions throughout the state, the program award represented his/her first opportunity to lead a research project as principal investigator. By program requirement, each of these grantees was supported by a senior colleague who agreed to serve as a mentor. Awards of up to $150,000 per year went a long way toward helping these young investigators establish a laboratory, assemble a core research team, and accumulate baseline data with the potential to launch a successful independent research career.

"The importance of the James and Esther King Biomedical Research Program support for our project cannot be overstated. It has allowed our group to start collaborative experiments that would not have been possible without the Team Science Program Grant."

— Dr. Mathias Salathe
University of Miami
2005 Team Science Program Grant

This collection of funded projects also provided meaningful opportunities during 2006 for 38 recent Ph.D.s to begin or continue their professional careers at Florida institutions and allowed 27 graduate students across the state to gain important experience as contributing research team members. Most spent 80 percent or more of their time on program sponsored research, and their salaries, fringe benefits, and tuition accounted for approximately 15 percent of the total program funds awarded during the year. After gathering exposure, interest, and expertise in research associated with tobacco-related disease, many of these predoctoral and postdoctoral students are more inclined to continue their research careers in Florida.

Grantee Profile

Ching-Jen Chen, Ph.D,

Florida State University, 2005 Small Business Technology Transfer Grant

Heart attacks, also known as myocardial infarction, occur when part of the heart muscle is damaged because it is not receiving enough oxygen. Like strokes, the time that elapses between the first sign of symptoms to receiving treatment is critical, and a few minutes can spell the difference between life and death. "In order to confirm that acute myocardial infarction has occurred, blood tests need to detect the presence of certain cardiac factors, which can take anywhere from 2 to 24 hours," explains Dr. Ching-Jen Chen. Dr. Chen, recipient of a 2005 Small Business Technology Transfer Grant, is developing a device that can shave hours off the time needed to reach a conclusive diagnosis.

Twelve years ago, Dr. Chen teamed up with a research partner, National High Magnetic Field Laboratory, to test a hypothesis about the effect of a magnetic field on blood cells. "I had several imaginative graduate students who were also intrigued by the idea, so I sent them to the lab to conduct some preliminary tests. They literally stuck their arms and legs into magnetic fields to determine what, if any, effect it would have on blood flow. They discovered that it slowed it significantly," he explains.

As any researcher will tell you, a new discovery often leads to a longer and more elaborate mode of inquiry. In 1996, Dr. Chen's discovery caught the attention of executives at Johnson & Johnson, who wanted to harness this technology to treat diseases of the white blood cells. For the following nine months, Dr. Chen's laboratory began testing the effect of a magnetic field to separate red and white blood cells. "We were discouraged because our original assumption — that iron ions within the red blood cells would migrate toward the magnetic field, thereby separating the cells — wasn't proving true. However, in spite of our confusion, we realized that nanomagnetic particles, which are less than a thousandth of the width of a human hair, could be attached to red blood cells, allowing clean separation of the two cell types. Until that point, no one had found a way to divide them in such a precise way." This new technology ultimately led to three new patents.

The team soon realized that nanomagnetics was not limited to diseases of the autoimmune system. With the help of a Small Business Technology Transfer Grant, Dr. Chen was able to devote his attention toward a new hypothesis — that nanomagnetic particles could be used to detect key proteins — known as cardiac factors — created by the body during episodes of acute myocardial infarction.

"Currently, as many as eight percent of patients seeking emergency care for chest pain are discharged, only to have a heart attack shortly thereafter," Dr. Chen points out. "This is particularly risky for patients whose early symptoms were mild because, if left untreated, the risk of having another heart attack soon afterward rises dramatically." As many as 65,000 Floridians currently suffer from coronary artery disease (CAD), the main cause of heart attacks, which is responsible for 400,000 deaths per year in the United States alone. Having a faster and more accurate means to identify heart attacks has the potential for dramatic effect on the lives of smokers, who suffer from CAD in disproportionately high numbers.

Dr. Chen's team was able to clearly identify and quantify four distinct cardiac factors present in very low concentrations during episodes of myocardial infarction. Because myoglobin, one of these factors, is produced in response to any muscle injury, it may or may not be indicative of a heart attack. However, the presence of other factors leads to a final diagnosis, allowing life-saving treatment to begin. Through their collaboration with a local startup company, Nanomagnetics and Biotech, Inc., Dr. Chen's team is now developing an inexpensive handheld device that requires only a small drop of blood and is capable of producing results in as little as fifteen minutes. His dream is to one day be able to develop a cell phone-sized device for use by paramedics and emergency room personnel.

Dr. Chen's device has also begun to show promise in detecting latex allergies in surgical patients and has the potential to reduce food-borne illness because it can be used to determine freshness. "The Small Business Technology Transfer Grant allowed us to further develop this technology, which has resulted in our fourth patent," he explains.

"Our research has allowed us to attract top-notch scholars to Florida State University, and we are now in a much better position to compete with major biomedical research centers in Massachusetts and California," he explains. "We're currently in the process of applying for a grant from the National Institutes of Health and have hired four new faculty members. Our ongoing collaboration with Nanomagnetics and Biotech, Inc. is facilitating a multidisciplinary dialogue with the potential to bring vast improvements to the current level of cardiac diagnosis and treatment, potentially saving untold numbers of lives."

Investment and Progress

Increasing Research Funding from Outside the State

Over the last year, researchers who have received funding from the program reported obtaining $7.7 million in additional funding directly related to their original James and Esther King grant project, and another $2.7 million that is indirectly related. As of October 2006, this brings the total amount of reported additional funding since program inception to more than $33 million. A list of awards reported by program grantees in 2006 appears in Appendix B.

"Funding from the James and Esther King Biomedical Research Program has provided the critical support needed to publish several high impact papers and enabled us to present our work at national and international scientific meetings. These research findings served as preliminary data for the preparation of an excellent NIH grant proposal that was funded. This funding supported our development and utilization of cutting edge techniques which will no doubt improve our chances of obtaining additional NIH funding."

— Dr. Mark McLean
University of South Florida
2004 Team Science Program Grant

Obtaining external funding typically hinges on the qualifications of the investigators. A key factor in judging a researcher's qualifications is the set of publications and presentations produced. Both number and caliber of publications carry weight in the larger scientific community, with the greatest credit given to peer-reviewed papers selected to be included in prominent journals. In recognition of this fact and out of a desire to disseminate the findings from research completed with its grants, the program strongly encourages awardees to publish their work on a timely basis. During 2006, past and current program grantees delivered at least 81 presentations in the United States and abroad on findings from program sponsored research. They also published 36 full articles in peer-reviewed biomedical journals, bringing the total number of publications to at least 176 since the program's inception. A list of publications collected over the past year is included in Appendix C.

Grantee Profile

William Self, Ph.D.

University of Central Florida, 2005 New Investigator Research Grant

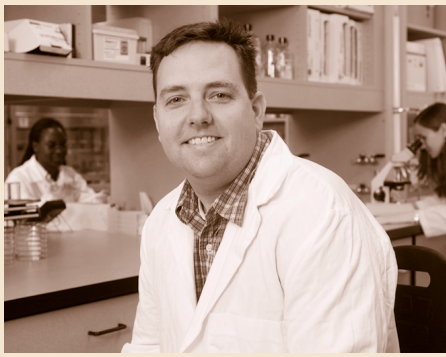
Considered the "toxic waste" of the body's oxygen metabolism, free radicals are extremely reactive and unpredictable molecules that initiate rapid chain reactions, which destabilize other molecules. Free radicals can damage lipids, proteins, and DNA, and can cause mutations that ultimately lead to cancer. However, for Dr. William Self, a biochemist at the University of Central Florida (UCF) and winner of a 2005 James and Esther King New Investigator Research Grant, the role of the micronutrient selenium may provide critical insight into the prevention of free radical damage.

Selenium is a common trace mineral found in a number of foods such as beef, poultry and seafood, as well as certain nuts and grains. "Important antioxidant enzymes are created when selenium is incorporated into proteins known as selenoproteins. We're currently looking at two distinct selenoproteins – thioredoxin reductase and glutathione peroxidase – which are essential in protecting cells from damage related to oxidative stress."

Arsenic, another metalloid, is a common geological by-product present in soil and groundwater, and a by-product of tobacco smoke. "The influence of arsenic on lung cancer is well established," Dr. Self explains. Arsenic is considered harmless in low doses; however, previous studies have correlated increased cancer rates (particularly lung cancer) in regions with higher levels of arsenic in drinking water. "A study published two years ago in the *Journal of the American Medical Association* showed that the risk for lung cancer increased dramatically in smokers with a higher arsenic intake."

Dr. Self's team is examining how arsenic impairs the cell's ability to synthesize selenoproteins properly, making the cell more susceptible to free radical damage. "My interest in selenoproteins was piqued when I began seeing studies on selenium metabolism and arsenic in 2000 and 2001. I was working as a post-doctoral fellow on selenium metabolism and bacterial selenoproteins at the National Institutes of Health, so investigating how cells transport, reduce and metabolize selenium in response to arsenicals seemed like a natural extension of that work when I arrived at UCF."

According to current Food and Drug Administration guidelines, the typical American diet is rich in selenium and often exceeds the minimum daily requirement. However, simply ingesting selenium-rich foods does not necessarily constitute a sufficiently potent therapeutic dose. Selenomethionine is currently available over-the-counter, but has not been shown to be effective in preventing the harmful effects of arsenic. Dr. Self's team is currently investigating different selenium compounds to see which is potentially the best form to counteract the negative effects of arsenic.



In trying to understand selenium's molecular implications, the team is staying in close contact with international research teams working to develop effective nutritional supplements. "There is a trial using either selenite or selenomethionine now underway in Bangladesh, where groundwater arsenic levels are dangerously high." Self's research also has the potential to fill a long-standing knowledge gap in the understanding of selenium metabolism. "Researchers have known that selenium metabolism was adversely affected by arsenic since the 1940's, but they just didn't know why," he explains. "Lung cancer has one of the poorest survival rates of all cancers, and preventing arsenic-induced lung damage would save innumerable lives. And, for smokers who can't kick the habit, we could at least potentially lower some of their risk for developing lung cancer."

"The New Investigator Research Grant was the first outside funding I'd received," Self explains. "Federal programs want to see success in getting competitive funding before they invest in your work. They want to see you will make good use of the money. The New Investigator Research Grant established me as a legitimate researcher and resulted in my recently being awarded NIH funding." Further, biomedical research funding has become much more difficult to obtain in the last decade as more researchers are competing for less funding. "Seven years ago, nearly a third of all proposals submitted got funding from the NIH, and now the number is closer to 20 percent. These types of programs are essential to help new scientists survive this tough period."

"In 2004, 12,360 Floridians died of lung cancer. However, with each new investigator helped by the James and Esther King Biomedical Research Program, Florida residents will continue to benefit from leading edge, life-enhancing treatments unavailable to previous generations. It's simply one of the most com passionate ways we can care for our citizens while continuing to broaden the scope of current scientific knowledge."

Investment and Progress

Stimulating Economic Activity Related to Biomedical Research

Indirectly, program investments during 2006 boosted the Florida economy by increasing the state's personal income, creating jobs, and generating subsequent tax revenue.[5] More directly, the program has dedicated a portion of the available funds every year since 2003 to stimulate the state's economy by funding tobacco-related projects with early potential to lead to commercial products or services through its Small Business Technology Transfer Grants. Over this period, the program has invested in nine partnerships between academic researchers and small businesses in the state, each jointly pursuing the feasibility of moving laboratory research into a commercial market. In addition, a number of the other funded research projects are producing results that may ultimately find a significant commercial market.

"The James and Esther King Biomedical Research Program is an outstanding and unique funding mechanism that has allowed us to obtain support and to address important questions relating to the effects of cigarette smoke on human biology and development. Without such a program, it would have been almost impossible to secure adequate funding for this critical research. We are deeply grateful to the program committee for the high standards set forth."

— Dr. Gianluca D'Ippolito
University of Miami
2004 New Investigator Reasearch Grant

For example, Dr. Richard Melker, recipient of a 2004 Small Business Technology Transfer Grant, used his award to test the use of cotinine to detect environmental tobacco exposure in exhaled breath. This project led him to conclude that, while cotinine was not a viable marker, the process itself held great promise. After developing a partnership with Convergent Engineering, this team has since been successful in obtaining Small Business Innovative Research (SBIR) Phase I and II awards totaling $600,000 from the National Science Foundation to further develop the signal processing technology, and $100,000 in SBIR Phase I funding from the National Institute of Alcohol Abuse and Alcoholism. The NIAAA grant supported a feasibility study of the testing device, and Dr. Melker expects to solicit Phase II support for its development.

Grantee Profile

James Dempsey, Ph.D.

University of Florida, 2004 New Investigator Research Grant

Since its inception in the late 1980s, clinicians and physicists have been working to develop a higher degree of accuracy in intensity modulated radiation therapy (IMRT), an advanced mode of radiotherapy using computer-controlled radiation beams to deliver precise doses to malignant tumors. The radiation is designed to conform to the three-dimensional shape of the tumor by optimally adjusting the strength and position of the beams, focusing a higher dose on the tumor while minimizing exposure to surrounding tissues.

Dr. James Dempsey, recipient of a 2004 New Investigator Research Grant, recognized the need for updating the programs used for proton radiation therapy. He is developing an advanced computer program that further increases the precision required to deliver a proton radiation dosage. Traditional radiation beams travel straight through the body, damaging all of the tissues in its path. Proton radiation, however, can be programmed to deliver most of its dose at the site of the tumor, preventing damage to surrounding tissues.

"I chose this project because it allowed a true collaboration between physicists and mathematicians to develop an optimal method to calculate the amount of radiation needed to treat head and neck cancer patients," Dr. Dempsey said. "Eighty percent of these cancers are the direct result of smoking, and advanced radiotherapy techniques such as proton therapy can prevent debilitating side effects while providing a good chance for a cure. For example, if we can preserve as much of the surrounding tissue as possible, preventing patients from having to lose their salivary glands during treatment for neck cancer, or causing blindness in the treatment of brain tumors, it dramatically improves the patient's quality of life."

Dr. Dempsey works closely with Dr. H. Edwin Romeijn, a mathematician with experience in designing large-scale optimization models, which are specially designed computer programs capable of producing a detailed, three-dimensional image of the body used to locate tumors. Their program improves on prior optimization models by paying particular attention to the problem of fluence map optimization, or FMO. Fluence maps are the checker board-like grid of radiation beams that surround the patient's body. FMO programs require a high level of accuracy if the beams are to be precise enough to kill tumor cells without harming surrounding tissue. Dr. Dempsey's team developed a series of extremely efficient algorithms that optimized photon beam placement in less than a minute's time.

Why is speed significant? "If clinicians can use the program to run a number of different optimization models quickly and easily, they are better able to remain focused on finding the best treatment plan possible," Dr. Dempsey explained. "In addition to the added speed and convenience, the program can also be run from a personal computer."

> "It's important that people know that these grants don't just benefit the researchers. They bring new jobs, business growth, and the advancement of new ideas — a whole new economy is being created out of this program."

"It's a great time to be in this field, and in Florida," Dr. Dempsey said. "In the past year, the University of Florida opened the Proton Therapy Institute, which is one of only four such centers in North America. Meanwhile, we were working on our large-scale optimization project right on the same campus. The time and energy that the New Investigator Research Grant allowed us to devote to research in optimized radiotherapy eventually led us to form our own company, ViewRay Inc. (http://www.viewray.com), which is a start-up based on an invention we disclosed to the University of Florida. ViewRay, Inc. has now grown to fourteen employees, and we're planning to release a commercial product in the near future. It's important that people know that these grants don't just benefit the researchers. They bring new jobs, business growth, and the advancement of new ideas — a whole new economy is being created out of this program. Since receiving a New Investigator Research Grant, I've also been able to secure funding from the National Institutes of Health and the National Science Foundation. The James and Esther King Biomedical Research Program saw the potential of our research early on, and we're grateful to them for having the foresight to help it grow."

2006 Grant Awards

Grant Mechanisms Offered

The program released a call for grant applications on December 15, 2005 for three types of grants that began July 1, 2006: New Investigator Research Grants, Small Business Technology Transfer Grants, and Team Science Program Grants.

"This program allows me to establish my own lab and generate exciting results. The generated data will enable my proposal to be competitive for national funding."

— Dr. Yanchang Wang,
Florida State University
2004 New Investigator Research Grant

New Investigator Research (NIR) Grants

The intent of the New Investigator Research Grant is to foster development of new Florida-based investigators by helping them undertake independent research that promises to become competitive for national research funding. Projects span a three-year period under the mentorship of a senior investigator, and proposals must address an important biomedical or behavioral problem relevant to tobacco-related disease.

Small Business Technology Transfer (SBTT) Grants

The purpose of the one-year Small Business Technology Transfer Grant is to help biomedical researchers at Florida universities or research institutions collaborate with Florida-based small businesses to initiate private sector commercialization of technology. The objective is to establish the technical/scientific merit and feasibility of the proposed research and development efforts so that the project may become competitive for further industry investment or national-level development funding, such as the federal Small Business Technology Transfer Research (STTR) program.

Team Science Program (TSP) Grants

The purpose of the Team Science Program Grant is to provide two years of support for broad-based, often multi-disciplinary research programs with well-defined major objectives or themes addressing the prevention, diagnosis, treatment, or cure of tobacco-related diseases that will result in an application at the national level to continue the research program over the long-term.

TSP projects generally involve the organized efforts of relatively large groups, members of which are conducting research projects designed to elucidate the various aspects or components of the overall objective. TSP grants consist of at least three, but no more than five, interrelated yet individual research projects directed toward well-defined research program goals.

Results of the 2006-2007 Call for Grant Applications

In response to "Call for Grant Applications FY 2006-2007", the program received 51 proposals. Seventy-eight percent of the applications submitted were for NIR grants, 12 percent for TSP grants, and 10 percent for SBTT grants. Requests for funding totaled $20,357,338. The program completed the application review and award process in June, and the Biomedical Research Advisory Council recommended funding 17 research grants totaling $8,091,596 beginning July 1, 2006. This action resulted in an overall proposal-to-award ratio of 33 percent.

Grant Mechanism	Applications Received	Applications Awarded	Percent of Applications Awarded
NIR	40	12	30%
SBTT	5	2	40%
TSP	6	3	50%
Total	**51**	**17**	**33%**

Table 1

2006-2007 Grant Applications Received/Awarded

Of the 2006 awards, 62 percent were NIR grants for distribution over a three-year term. Approximately 35 percent of the total funding awarded was for TSP grants for distribution over two years, while the remaining two percent of funding were for one-year SBTT grants. In all cases of multi-year eligibility, continued funding is conditional upon acceptable grantee performance in each year of research as well as the availability of funds.

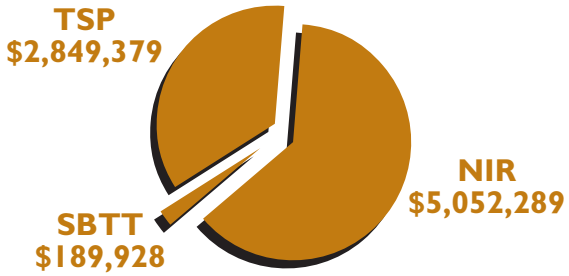


Figure 4

Value of 2006-2007 Grants Awarded by Mechanism

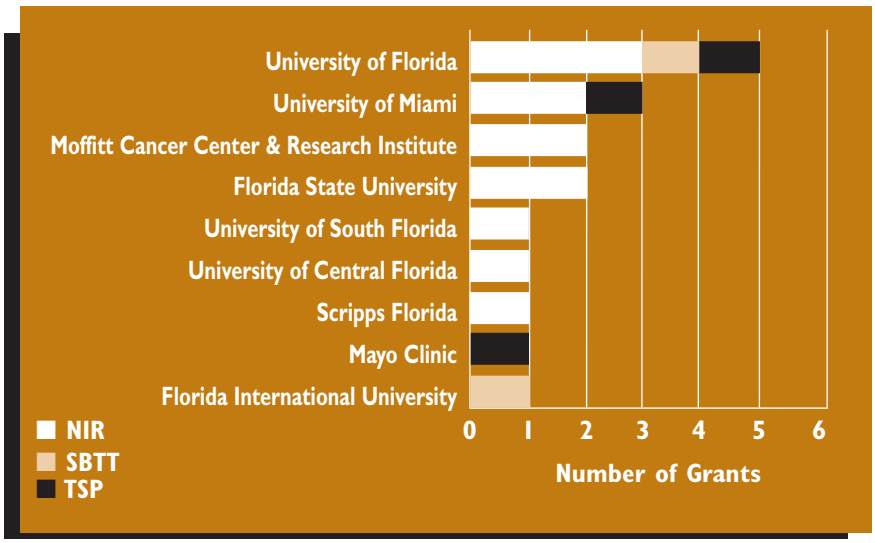


Figure 5

Number of 2006-2007 Grants Awarded by Institution

The program awarded grants to researchers at nine Florida research institutions, with researchers at the University of Florida and the University of Miami accounting for eight of the 17 awards, or 47 percent, distributed in 2006.

New Grants Awarded in 2006

The following is a list of the 17 new research projects awarded grants in 2006, totaling $8,091,596. An abbreviated abstract of each researcher's funded project appears in Appendix D.

New Investigator Research Grants

Mark Alexandrow, Ph.D.
H. Lee Moffitt Cancer Center & Research Institute
Functional Role of Mcm7-Rb Interactions in Ras Signaling and Tumorigenesis
$427,500

Suzanne Cappendijk, Ph.D.
Florida State University
Acute and Long-Term Behavioral and Neurological Effects of Nicotine in the Zebra Finch
$383,889

Li-Mei Chen, M.D., Ph.D.
University of Central Florida
Prostasin Protects Lung Epithelial Cell Integrity from Cigarette Smoke Induced Stress
$427,500

Bradley Fletcher, M.D., Ph.D.
University of Florida
Transposon-mediated Targeted Thrombosis of Tumor Vasculature
$427,500

Stephen Grobmyer, M.D.
University of Florida
Metabolically Targeted Nanoshells for High Resolution In Vivo Imaging of Cancer with Finite Element Based Photoacoustic Tomography
$427,500

Lin Liu Ph.D.
University of South Florida
Telomere Susceptibility to Cigarette Smoke-Associated Chromosomal Abnormalities in Embryos
$427,500

Hendrick Luesch, Ph.D.
University of Florida
The Mode of Action of the Antitumor Agent Apratoxin A
$427,500

Dana Rollison, Ph.D.
H. Lee Moffitt Cancer Center & Research Institute
Case-Control Study of Smoking and Human Papillomavirus Infection in Basal and Squamous Cell Carcinomas of the Skin
$401,820

Layton Smith, Ph.D.
Scripps Florida
The Interaction Between Apelin and the Renin-Angiotensin-Aldosterone System
$427,500

Hengli Tang, Ph.D.
Florida State University
Mechanism of HCV Resistance to Cyclosporine A
$427,500

Roberto Vazquez-Padron, Ph.D.
University of Miami
The Role of Nicotine in Smoking-Related Vascular Diseases
$427,500

Ewa Wojcikiewicz, Ph.D.
University of Miami
Biophysical Determinants of Leukocyte Transmigration
$419,080

Small Business Technology Transfer Grants

Jonathan Li, Ph.D.
University of Florida
Eliminating Targeting Errors in Lung Cancer Radiotherapy Using Time-Resolved Volumetric Magnetic Resonance Imaging
$95,000

Anthony McGoron, Ph.D.
Florida International University
A Micro-Fabricated In Vivo Bubble Oxygenator for the Treatment of Induced Severe Pulmonary Disease
$94,928

Team Science Program Grants

Paul Davenport, Ph.D.
University of Florida
The Role of Nicotine in the Neural Control of Respiratory and Cardiovascular Systems
$949,404

Alan Fields, Ph.D.
Mayo Clinic
Oncogenic PKC Iota in Smoking-Related Lung Cancer
$950,000

David Lee, Ph.D.
University of Miami
Reducing the Burden of Tobacco-Associated Cancers in Florida
$949,974

National Biomedical Research Funding and Funding Trends

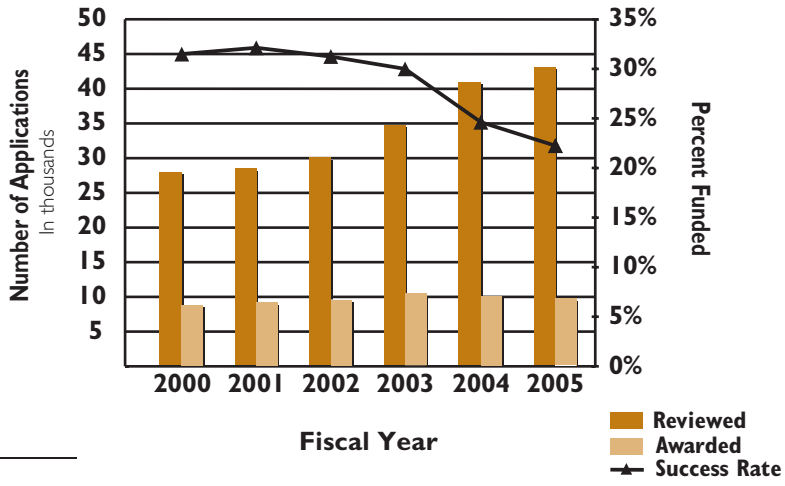
In a 2005 national survey conducted of senior research administrators in 35 states (including Florida), 92 respondents indicated that the most important trend affecting the overall research environment in the United States is the decline in federal funding. "This trend was mentioned by 40 percent of respondents – more than four times more frequently than any other trend, positive or negative." [6]

There are two important factors contributing to this trend. First, since 2003, absolute budget cuts and the biomedical inflation have produced a 10 percent reduction in overall NIH purchasing power.[7] Second, since 2001, the number of applications for individual investigator-initiated research grants has steadily increased. These two factors have combined to cause the likelihood of success in earning NIH funding to plummet (Figure 6).

The Biomedical Research Advisory Council and program staff continue to monitor the research priorities of the National Institutes of Health as embodied in its "Roadmap for Medical Research: New Pathways to Discovery" (cellular, molecular, and atomic level technologies), "Research Teams of the Future" (interdisciplinary collaboration), and "Re-engineering the Clinical Research Enterprise" (translating laboratory discoveries into clinical practice). As you may read elsewhere in this report, a large number of our current grants support work in these areas. These priorities can be expected to continue guiding future program planning and project selection.

Figure 6

Trend in Funding from National Institutes of Health[8]



Florida researchers succeeded in winning just over $331 million from NIH in FY 2006; this figure represents a decline of $36 million from the prior year. While Florida ranked 18th among all 50 states for the year in total percent of NIH funding received, it remains among the lowest in the nation (45th) on a per capita basis (see Appendix E).

Although funding from the National Institutes of Health was by far the largest component of biomedical research grants awarded to Florida researchers in 2006, investigators across the state earned support from a number of other national programs as well, a few of which are reported in Figure 7.

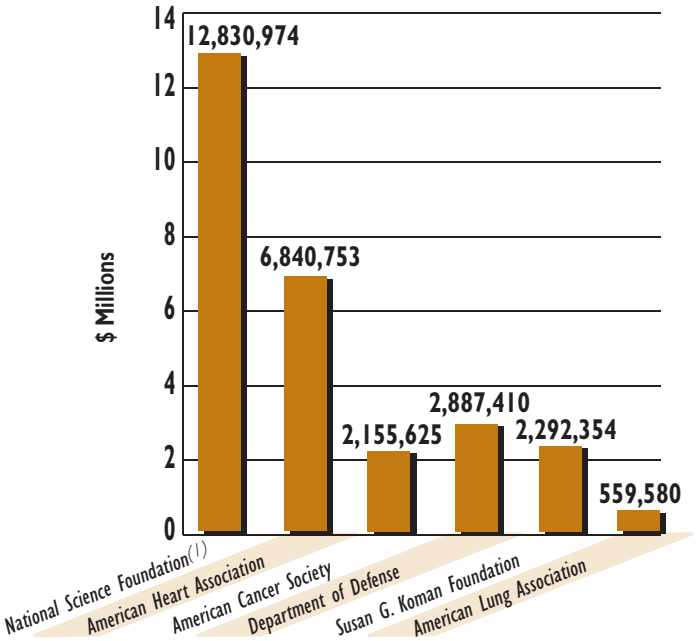


Figure 7

Select 2006 National Biomedical Research Awards in Florida

(1) 2005 funding estimated based on data from prior years

The Biomedical Research Advisory Council

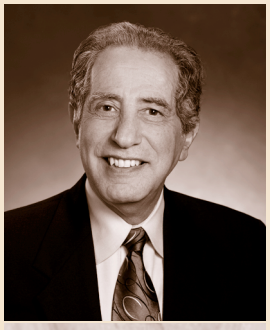
In section (s.) 215.5602 *Florida Statutes (F.S.)*, the Florida Legislature established the Biomedical Research Advisory Council within the Department of Health and defined its authority (see Appendix F). In 2006, they revised this statute to expand the advisory council from nine to 11 members to support the newly created Bankhead-Coley Cancer Research Program. The advisory council consists of the following delegates:

- One representative of the Florida Division of the American Cancer Society
- One representative of the Florida/Puerto Rico Affiliate of the American Heart Association
- One representative of the American Lung Association of Florida
- Four members appointed by the Governor
  - Two members with expertise in the field of biomedical research
  - One member from a research university in the state
  - One member representing the general population of the state
- Two members appointed by the President of the Florida Senate
  - One member with expertise in the field of behavioral or social research
  - One representative from a cancer program approved by the American College of Surgeons
- Two members appointed by the Speaker of the House of Representatives
  - One member from a professional medical organization
  - One representative from a cancer program approved by the American College of Surgeons

By law, the advisory council makes grant award recommendations to the Secretary of the Department of Health for tobacco-related research through the James and Esther King Biomedical Research Program. Among its other responsibilities, the advisory council also advises the Secretary and the Office of Public Health Research as to the direction and scope of the program and assists in the development of guidelines to ensure fairness, neutrality, and adherence to the principles of merit and quality in the conduct of its operation.

During 2006, seven new members were appointed to the advisory council, each serving three-year terms. The following list names the members and the seats they hold:

Biomedical Research Advisory Council Members

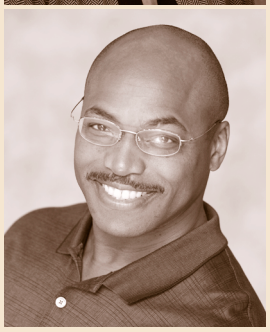


Edward R. Block, M.D.
Distinguished Professor and Chair
Department of Medicine
University of Florida
Seat: American Lung Association
Appointed: July 1, 2000

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

Nikolaus S. Gravenstein, Ph.D.
Professor and Chair
Department of Anesthesiology
University of Florida
Seat: Biomedical Research
Appointed: February 27, 2006

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



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

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

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

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

Mary Lou Sole, R.N., Ph.D.,
C.C.R.N., F.A.A.N.
Professor, School of Nursing
College of Health and
Public Affairs
University of Central Florida
Seat: House -
Professional Medical Organization
Appointed: February 27, 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

VACANT
Seat: House – Cancer Program (ACoS)

Program Operations

Summary of Program Funding History

Funding for the program comes from the interest earned on a $150 million reserve within the Lawton Chiles Endowment Fund, a fund established with monies received from the tobacco industry through Florida's tobacco lawsuit settlement. In 2004, enhanced funding was appropriated through a distribution from alcoholic beverage surcharge taxes. In 2006, Governor Jeb Bush and the Florida Legislature substituted a six million dollar annual appropriation commitment through 2010 to the Biomedical Research Trust Fund within the Department of Health for purposes of the James and Esther King Biomedical Research Program.

Table 2 below outlines the number of grant applications received and the number, type, and total value of grant awards extended for each of the six years the program has been in existence. Forty-two inaugural grants were awarded in fiscal year 2001. Appropriations through FY 2003-04 were used to fulfill multi-year continuation awards to these grantees, where appropriate. Except for three one-year Small Business Technology Transfer Grants totaling $150,000 and funded from administrative expenses, no new grants were awarded until FY 2004-05.

Pursuant to s. 20.435, *F.S.*, beginning in FY 2004-05 grant money that is obligated but not disbursed by the end of the fiscal year may be carried forward to pay out multi-year grants in subsequent years.

Table 2

Program Award History

	FY 2001-02		FY 2002-03		FY 2003-04		FY 2004-05		FY 2005-06		FY 2006-07	
Applicants	189		No Call		55		57		44		51	
Awards	**No.**	**Million**	**No.**	**Million**	**No.**	**Million**	**No.**	**Million**	**No.**	**Million**	**No.**	**Million**
IIR	28	9.08			n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
NIR	14	7.37			0	0	13	5.62	11	4.85	12	5.05
SBTT	n/a	n/a			3	0.15	2	0.20	2	0.20	2	0.19
TSP	n/a	n/a			n/a	n/a	3	2.91	3	2.99	3	2.85
Totals:	***42***	***$16.45***	***0***	***$ 0***	***3***	***$0.15***	***18***	***$8.73***	***16***	***$8.04***	***17***	***$8.09***

** above numbers are rounded*

Administrative Costs

Administrative costs are limited to 15 percent of the amount appropriated. As the data shown below indicate, program staff has held administrative costs below the legislative limit, freeing up more dollars for research project support.

Table 3

Program Expenditures ($ Million)[a]

Fiscal Year	Appropriation	Grant Awards	Percent	Administrative Expenses	Percent
FY 06-07	9.50	8.09	85%	n/a	-
FY 05-06	9.37	8.04	86%	0.67	7%
FY 04-05[b]	9.40	8.73	93%	0.68	7%
FY 01-04	17.64	16.45	93%	0.87	5%
Total	**45.91**	**41.31**	**90%**	**2.22[c]**	**6%**

[a] The value of grant awards and administrative expenses may be less than the annual appropriation. Excess funds stay in the Biomedical Research Trust Fund and are available for future use by the program.

[b] Beginning with FY 2004-05 administrative expenses include $250,000 for the Center for Universal Research to Eradicate Disease pursuant to s. 215.5602 (12), *F.S.*

[c] Calculation excludes FY 2006-07

Program Administration

The Secretary of the Florida Department of Health has designated the Office of Public Health Research to carry out the department's responsibility for overseeing the administration of the program. Within this office, a program manager is responsible for:

- Working with the advisory council to develop program policy, research grant programs and initiatives, evaluate program effectiveness, and review long-term goals
- Managing the budget to ensure appropriate use of trust fund monies
- Procuring and managing any service contracts
- Overseeing the award and payment process
- Monitoring existing grants for progress and use of funds

As a contracting partner, Lytmos Group provides the following services to the program:

- Program Development—Funding cycle and call for grant applications preparation, development and refinement of program policies and procedures and program materials
- Application Processing—Acceptance and processing of online applications, including administrative review for compliance with call requirements
- Peer Review Management—Reviewer recruiting, panel and review assignments, and development of evaluation materials
- Decision Support—Competition analysis and reporting, funding decision aides, and Biomedical Research Advisory Council support
- Administrative and Programmatic Monitoring—Financial and progress report evaluations; site-visits; awardee compliance with human and animal use assurances; grantee support for project, budget, or key personnel changes; financial and scientific overlap monitoring; and continuation request processing
- Program Evaluation and Improvements—Ongoing monitoring and implementation of process and performance enhancements
- Technical Support—Web site development and maintenance, automated application processing grant management systems support, and grantee technical assistance

The Granting Process for FY 2006-07

The 2006 grant process began with guidance from the advisory council on grant mechanisms and eligibility requirements to be included in "Call for Grant Applications FY 2006-07."

Program staff twice notified more than 500 interested parties by e-mail of 2006 funding opportunities, and posted information on the program web site www.floridabiomed.com. They collected written questions from applicants and published answers on the program web site for the benefit of all candidates. Applicants completed online applications tailored for each grant mechanism. After the application deadline, Lytmos Group arranged for experienced scientists from outside the state of Florida with specific expertise in the application topics to independently peer review each application, assign a score based on technical merit, and assess the relationship to tobacco-related disease. To compensate for the fact that reviewers did not engage in a discussion and to arrive at consensus on an overall rating, Lytmos excluded the high and low scores before averaging the remaining scores to create each proposal's final peer review rating and then rank ordered the set of applications. At the advisory council meeting in May 2006, program staff presented this data in a manner that was blind to the identity of the investigator and institution in order to avoid conflicts of interest. The advisory council then considered overall program objectives in establishing priorities and fundable ranges for each grant mechanism.

After making funding recommendations to the Secretary, the advisory council examined details regarding the peer review process, including the curriculum vitae of the reviewers, review assignments, and individual evaluation reports to ensure that the quality of the process met program standards. Program staff completed a final check of eligibility requirements during June, and new awards were effective July 1, 2006.

Grant Management

During 2006, the program ensured integrity and accountability in its grant award and administrative processes by:

- Requiring quarterly financial reports and monitoring spending patterns
- Requiring grantees to justify expenditures and proposed changes to budgets, key personnel, and research protocols
- Requiring annual progress reports and subjecting them to peer review
- Conducting grantee site visits
- Providing technical assistance as needed

Grantees and their institutions are accountable to the program for properly administering the sponsored activities in accordance with applicable regulations and policies and the award "Terms and Conditions."

With the understanding that research by its very nature is unpredictable, the program has high expectations of its grantees to complete the planned project aims. One of the central tools used by the program in communicating research plans and reporting progress is the "Research Milestone Chart." Developed by each grant candidate, this chart shares the planned high-level schedule for each stated project aim and includes major milestones over the life of the project. The rationale for introducing this tool is that effective project planning by the principal investigator is an essential requirement for a successful project. In addition to helping the application reviewer understand the project timeline, the "Research Milestone Chart" serves as the frame of reference for the grant manager and other program staff during the project period.

In written progress reports, principal investigators describe the status of their work relative to the specific aims and milestone chart contained in their project proposal and share significant findings to date. They also present plans for addressing unanticipated outcomes or project delays and report project-related published works, patents, and complementary funding. During 2006, all active grantees provided these reports in mid-April. Sets of three subject matter experts from outside the state peer reviewed each of these reports for reasonableness, and in many cases offered helpful suggestions. Each principal investigator received a copy of his/her peer review evaluation and were given an opportunity to respond to reviewer comments.

Site visits, typically conducted once during the life of a grant, allow program staff to meet the investigators and sponsored research personnel, see and hear more about progress in the projects, and ensure that proper institutional controls are in place to support the state's investment. Of nearly equal importance, these visits provide an opportunity to gather feedback from current and future grantees about the program that helps enhance policy-making and administrative oversight. Following a prescribed format, the site visit team examines institutional policies and controls, and principal investigators conduct lab tours and make presentations on their research followed by question-and-answer sessions. Grantee mentors, project team members, and other institution staff attend. At the conclusion of the visit, the site team shares preliminary findings in a closing meeting and follows up with a written site visit report that includes any necessary corrective actions.

During 2006, program staff conducted site visits with 12 of the 2004 and 2005 grantees at the University of Florida, Mayo Clinic, University of South Florida, and H. Lee Moffitt Cancer Center & Research Institute.

Grant Continuation Process

Multi-year awardees must submit formal requests to renew their grants on an annual basis. Continuation funding is contingent upon evidence of acceptable progress towards the project aims and research milestones, including narrative progress report and associated peer review, principal investigator response, the "Research Milestone Chart" and site visit information. If progress is significantly lacking, the principal investigator must provide a reasonable recovery plan in order to receive subsequent funding.

After reviewing all available information, the grant manager recommends continuation, conditional continuation, or grant termination. A non-conflicted subcommittee of the advisory council examines each case involving grant manager recommendations for conditional continuation or termination; this subcommittee arrives at a consensus recommendation to program staff for each case.

During 2006, this process led to program decisions not to renew one multi-year grant and to suspend further disbursements on another grant pending evidence of improved progress in an interim report. However, based on evidence of satisfactory progress, the program granted requests for the next year of funding for the other 25 multi-year awardees.

Recommendation for Policy Change

In order to enhance the program's ability to achieve the goals spelled out in s. 215.5602, *F.S.*, the Biomedical Research Advisory Council offers the following recommendation for changes to current policy:

Stagger the appointments to the Biomedical Research Advisory Council in order to maintain continuity in institutional knowledge in advising the program.

With a turnover of six seats and the addition of two new seats during 2006, the program relied heavily on the three incumbent representatives of the American Heart Association, American Lung Association, and American Cancer Society to represent the history and past practices of the advisory council to seven new members. On multiple occasions, scheduling conflicts prevented one or more of these members from participating in council meetings. When faced with making key program recommendations, new members experienced extraordinary demands to absorb historical information or proceeded with limited insight into past council rationale.

Appendix A Grants Active in 2006 by Research Topic

The list presents the diverse collection of behavioral and biomedical research projects active in 2006, including a very brief description of the project, the name of the principal investigator, and the initial year of award. While many projects may be classified in multiple categories, this list assigns each project to one significant association. Complete project abstracts are available on the program website, www.floridabiomed.com.

Tobacco Addiction

Prevention

- Use of the zebra finch to study behavioral and neuronal changes caused by nicotine (Susanne Cappendijk, 2006).
- The effects of eliminating a youth targeted, anti-tobacco prevention program (Noella Dietz, 2005).
- Epidemeology study to determine areas of Florida where anti-smoking programs and treatments are most needed (David Lee, 2006).

Treatment/Cure

- Possible use of neurotensin analogs to treat nicotine dependence (Mona Boules, 2004).
- The potential use of cannabinoid antagonists in the treatment of nicotine dependence (Ceylan Isgor, 2005).

Specific Tobacco-Related Diseases

Cardiovascular Disease (including Stroke)

Prevention

- The role of blood pressure changes, endothelial cell function and inflammation in renal failure (Richard Johnson, 2005).

Diagnosis

- Development of a small, rapid detection device for measuring cardiac markers of myocardial infarction at the point of contact (Ching-Jen Chen, 2005).

Treatment/Cure

- Improvement of balance with home exercise programs (Mark Bishop, 2004).
- The use of a white matter stroke model to study the role of neurotrophic factors and electrical activity in ischemic axonal injury (Jeffrey Goldberg, 2005).
- The regulation of GABA transporter GAT-1 during ischemia (Christof Grewer, 2004).
- The possible use of human mesencymal stem cells in production of by-pass grafts for human transplant (Teng Ma, 2004).
- Nicotine effects on hormonal regulation of cholesterol (Mark McLean, 2004).
- The potential use of autologous myoblasts in patients with end-stage heart failure awaiting heart transplantation (Daniel Pauly, 2004).
- The interaction between apelin and the renin-angiotensin-aldosterone system (Layton Smith, 2006).
- The role of nicotine in vascular smooth muscle disease (Roberto Vazquez-Padron, 2006).
- Leukocyte transmigration and endothelial cell function in atherosclerosis (Ewa Wojcikiewicz, 2006).

Pulmonary Disease

Prevention

- The prenatal and postnatal effects of nicotine on neural control mechanisms of the respiratory and cardiovascular systems (Paul Davenport, 2006).

Treatment/Cure

- The role of prostatin and DNA methylation in lung epithelium (Li-Mei Chen, 2006).
- A microfabricated bubble oxygenator to treat patients with severe pulmonary disease (Anthony McGoron, 2006).
- The effects of tobacco-induced reactive oxygen species on bronchial mucous production and disease (Matthias Salathe, 2005).
- Nitrous oxide and lung damage via nitrosylation with tobacco smoke (Antony Veena, 2004).
- Effect of smoke on the CAT-1 L-Arginine transporter and the production of nitrous oxide in pulmonary endothelial cells (Sergey Zharikov, 2004).

Cancer

Prevention

- LBH gene expression as a regulator of embryonic development (Karoline Briegel, 2005).
- Protective role of selenium against arsenic-induced lung cancer (William Self, 2005).
- The mechanism of drug resistance to cyclosporine A treatment in hepatitis C induced liver cancer (Hengli Tang, 2006).

Diagnosis

- The use of flow cytometry for more accurate screening of pleural fluids from patients suspected of having lung cancer (Atwar Ganju-Krishan, 2005).
- The use of genomics to develop a lab test to detect bladder cancer in urine (Charles Rosser, 2005).
- Potential use of a test for DNA methylation to predict cervical cancer risk in smokers with HPV infection (Erin Siegel, 2005).

Treatment/Cure

- Functional role of Mcm7-Rb in Ras signaling and tumorgenisis (Mark Alexandrow, 2006).
- Use of VSV viruses as anti-tumor agents (Glen Barber, 2004).
- Identification of proteins involved in lung cancer neovasculogenesis (Christopher Cogle, 2005).
- Integrative approaches to improving patient outcomes in renal cell carcinoma (John Copland, 2005).
- Enhanced computer programs to optimize proton radiation therapy treatments (James Dempsey, 2004).
- Medicinal chemistry and synthesis of roseophilin and related anti-tumor compounds (Gregory Dudley, 2005).
- Oncogenic role of PKC iota in smoking-related lung cancer (Alan Fields, 2006).
- The use of fusion proteins to selectively target and induce thrombosis and occlusion of tumor vasculature (Bradley Fletcher, 2006).
- The role of the G-strand overhang in telomerase activity and function (Terace Fletcher, 2004).
- The use of nanoshells as vehicles for drug delivery, as contrast media, and in thermo ablation therapy (Stephen Grobmyer, 2006).
- Tumor suppressive function of Daxx in tobacco-mediated breast malignancy (Alexander Ishov, 2005).
- The role of laminins in angiogenesis and invasion of squamous cell carcinoma (Jie Li, 2004).
- Improving lung cancer radiation therapy through the use of real-time MRI to track movement (Johnathan Li, 2006).
- STAT3 protein involvement in the mechanism of the anti-tumor agent apratoxin A (Hendrik Luesch, 2006).
- Purine-induced down-regulation of XIAP inhibitors of apoptosis (Subhara Mohapatra, 2004).
- Development of a vaccine against lung cancer using gp-96 fusion proteins (Luis Raez, 2005).
- Effect of smoking on skin cancer risk in patients with HPV infection (Dana Rollison, 2006).
- Mutations in phosphotase 2A result in DNA damage and a failure to regulate cell division (Yanchang Wang, 2004).

Tobacco-Related Effects on Other Human Systems

Treatment/Cure

- Molecular mechanisms involved in nicotine's effect on steroidogenisis and reproduction (Himangshu Bose, 2004).
- Hypoxia induced inhibition of bone formation through the PI3K/AKT signaling pathway (Gianluca D'Ippolito, 2004).
- The effect of smoking on telomere function and its correlation with infertility and developmental abnormalities (Lin Liu, 2006).

Appendix B Related Awards Reported by Grantees

The following list represents **$7,733,881** in additional single and multi-year research awards reported since October 2005 by current and past grantees that are based directly on research findings from projects funded by the James and Esther King Biomedical Research Program. Grants are presented in alphabetic order by last name of the principal investigator, with the King award year and type listed in parentheses.

Copland, **J**. (2005 TSP), "Type II TGF Beta Receptor and RCC Progression," National Cancer Institute, $250,000.

Dempsey, **J**. (2004 NIR), "Intensity Modulated Radiation Therapy: Integrated Models and Algorithms," National Science Foundation, $160,000.

D'Ippolito, **G**. (2004 NIR), "Mechanisms of Marrow Stromal Stem Cell Self-Renewal," Veterans Administration Research Service, $1,003,600.

Fletcher, **T**. (2004 NIR), "Structural Analysis of Telomere Chromatin," Predoctoral Fellowship to Asmaa Baker, National Institutes of Health, $145,000.

Ganju-Krishan, **A**. (2005 SBTT), "Body Cavity Cell Analysis," Women's Cancer Research Association, $50,000.

Ganju-Krishan, **A**. (2005 SBTT), "Flow Analysis Workshop," Indo-US Science and Technology Forum, $30,000.

Magleby, **K**. (2001 IIR), "Engineered Bio-Molecular Nano-Deviced Systems," Electronic Biosciences, $293,202.

McLean, **M**. (2004 TSP), "Molecular Basis for the Differential Regulation of SR-B Isoforms by Estrogen," National Heart, Lung, and Blood Institute, $1,408,212.

Melker, **R**. (2004 SBTT), "Dynamic Signal Processing and Information Extraction for E-Noses," National Science Foundation, $600,000.

Melker, **R**. (2004 SBTT), "Electronic Nose Medical Compliance Monitor," National Institute on Alcohol Abuse and Alcoholism, $100,000.

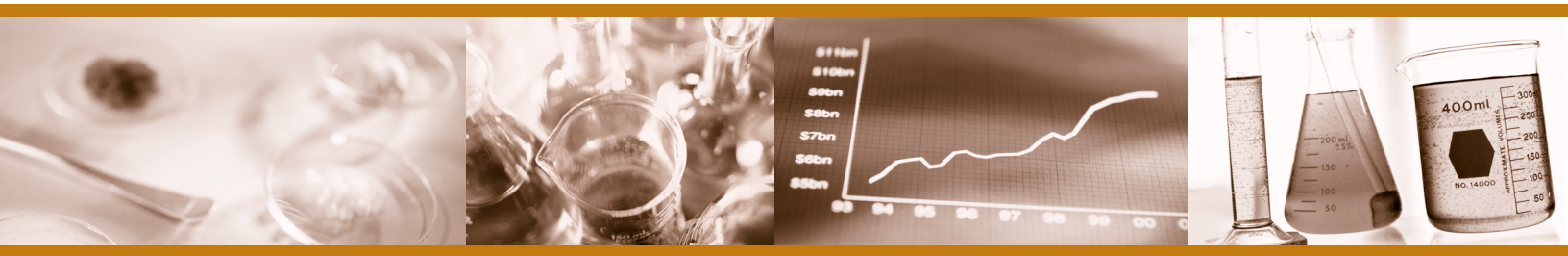
Salathe, **M**. (2005 TSP), "Ciliary Dysfunction in ETS-Induced Bronchitis," Flight Attendants Medical Research Institute, $325,492.

Salathe, **M**. (2005 TSP), "Regulation of Airway Lactoperoxidase Host Defense," National Heart, Lung, and Blood Institute, $1,754,375.

Salathe, **M**. (2005 TSP), "Molecular Regulation of the Foxj1 Gene, Control of Ciliated Epithelial Cell Differentiation," American Lung Association of Florida, $150,000.

Self, **WT**. (2005 NIR), "Impact of Arsenicals on Selenoprotein Synthesis," National Institute of Environmental Health Sciences, $214,000.

Wecker, **L**. (2001 IIR), "Regulation of Neuronal Nicotinic Receptors," National Institute on Drug Abuse, $1,250,000.



Since October 2005, current and past grantees reported **$2,738,390** in awards that are not based directly on research findings from projects funded by this program. However, having the James and Esther King award enhanced their competitiveness in earning this additional funding. Grants are presented in alphabetic order by last name of the principal investigator, with the King award year and type listed in parentheses.

Ames, **S**. (2001 NIR), "Quality of Life Intervention for Biochemical Recurrence of Prostate Cancer," Lance Armstrong Foundation, $247,500.

Bishop, **M**. (2004 NIR), "Faculty Opportunity Fund: Developing a Model of Endogenous Low Back Pain," University of Florida, $87,350.

Boules, **M**. (2004 NIR), "NT69L: A Potential, Novel Antischizophrenic Drug," National Institutes of Health, $1,490,000.

Briegel, **K**. (2005 NIR), "Deregulation and Function of T Box Factor 2 (TBX2) in Neoplastic Mammary Gland Development," University of Miami Sylvester Cancer Center, $50,000.

Ma, **T**. (2004 NIR), "GAP: Perfusion Bioreactor System for Stem Cell Expansion," Florida State University, $40,000.

Ma, **T**. (2004 NIR), "Predoctoral Award: Energy Metabolism of hMSC in a Perfusion Bioreactor as They Differentiate into Cardiomyocyte," American Heart Association Florida Affiliate, $43,540.

Rosser, **C**. (2005 NIR), "Mycoplasma Association with Tumor Invasion," American Cancer Society, $680,000.

Self, **WT**. (2005 NIR), "Biologically Compatible Engineered Nanoparticles to Prevent UV-Radiation Induced Damage," National Science Foundation, $100,000.

Appendix C Grantee Publications

The following list represents new publications in peer-reviewed journals and books based on funded research that current and past program grantees have reported since October 2005. 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.

Su Y, Zhang J, Patel JM, **Antony V**, Block ER. Concentration-dependent effects of nitric oxide on angiogenesis of lung microvascular endothelial cells: role of calpain nitrosylation. *Proc Am Thorac Soc*. 2006; 3(6):548-549.

Barber GN. The dsRNA-dependent protein kinase, PKR and apoptosis. *Cell Death Differ.* 2005; 12(6):563-70.

Barber GN. VSV-tumor selective replication and protein translation. *Oncogene.* 2005; 24(52):7710-19.

Kondrikov D, Han HR, **Block ER**, Su Y. Growth and density-dependent regulation of NO synthase by the actin cytoskeleton in pulmonary artery endothelial cells. *Am J Physiol Lung Cell Mol Physiol*. 2006; 290(1):L41-L50.

Su Y, Cui Z, Li Z, **Block ER**. Calpain-2 regulation of VEGF-mediated angiogenesis. *FASEB J*. 2006; 20(9):1443-1451.

Qiu K, Su Y, **Block ER**. Use of recombinant calpain-2 siRNA adenovirus to assess calpain-2 modulation of lung endothelial cell migration and proliferation. *Mol Cell Biochem.* 2006; 292(1-2):69-78.

Boules M, Iversen I, Oliveros A, Shaw A, Williams K, Robinson J, Fredrickson P, Richelson E. The neurotensin agonist, NT69L, suppresses sucrose-reinforced operant behavior in the rat. *Brain Res*. 2006; Nov 16 [EPub].

Boules M, Fredrickson P, Richelson E. Bioactive analogs of neurotensin. *Peptides.* 2006; 27(10):2523-2533.

Briegel KJ. Embryonic transcription factors in human breast cancer. *IUBMB Life*. 2006; 58(3):123-132.

Fox D, Romeijn HE, **Dempsey JF**. Fast voxel and polygon ray-tracing algorithms for IMRT treatment planning. *Med Phys*. 2006; 33(5):1364-71.

Li H, **Dempsey JF**. A Fourier analysis on the maximum acceptable grid size for discrete proton beam dose calculation. *Med. Phys.* 2006; 33(9):3508-18.

Romeijn HE, Ahuja RK, **Dempsey JF**, Kumar A. A new linear programming approach to radiation therapy treatment planning problems. *Operations Research.* 2006; 54(2):201-216.

D'Ippolito G, Diabira S, Howard GA, Roos BA, Schiller PC. Low oxygen tension inhibits osteogenic differentiation and enhances stemness of primitive human MIAMI cells. *Bone*. 2006; 39(3):513-22.

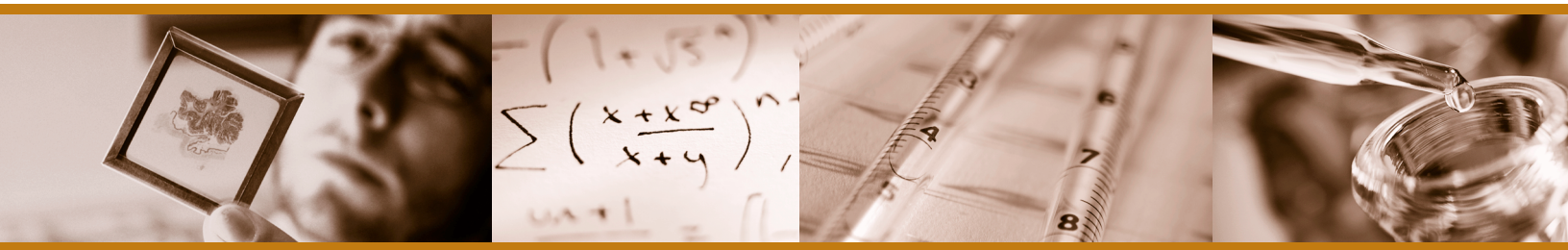
D'Ippolito G, Howard GA, Roos BA, Schiller PC. Isolation and characterization of marrow-isolated adult multilineage inducible (MIAMI) cells. *Exp Hematol*. 2006; 34(11):1608-10.

D'Ippolito G, Howard GA, Roos BA, Schiller PC. Sustained stromal stem cell self-renewal and osteoblastic differentiation during aging. *Rejuvenation Res*. 2006; 9(1):10-19.

Elliot S, Karl M, Berho M, Xia X, Pereria-Simon S, Espinosa-Heidmann D, Striker G. Smoking induces glomerulosclerosis in aging estrogen deficient mice through cross-talk between TGF-beta 1 and IGF-1 signaling pathways. *J Am Soc Nephrol*. 2006; 17(12):3315-24.

Faria AMC, Levay A, Wang Y, Kamphorst AO, Rosa MLP, Nussenzveig DR, Balkan W, Chook YM, Levy DE, **Fontoura BMA**. The nucleoporin Nup96 is required for proper expression of interferon-regulated proteins and functions. *Immunity*. 2006; 24(3):295-304.

Forteza R, Casalino-Matsuda SM, Monzon ME, Fries E, Rugg MS, Milner CM, Day AJ. TSG-6 potentiates the anti tissue kallikrein activity of inter-{alpha}-inhibitor through bikunin release. *Am J Respir Cell Mol Biol*. 2006; Jul 27 [Epub].



Casalino-Matsuda SM, Monzon ME, **Forteza RM**. Epidermal growth factor receptor activation by epidermal growth factor mediates oxidant-induced goblet cell metaplasia in human airway epithelium. *Am J Respir Cell Mol Biol.* 2006; 34(5):581-91.

Krishan A, Ganjei-Azar P, Jorda M, Hamelik RM, Reis IM, Nadji M. Detection of tumor cells in body cavity fluids by flow cytometric and immunocytochemical analysis. *Diagn Cytopathol*. 2006; 34(8):528-541.

Lopez D, **Ness GC**. Characterization of the rat LDL receptor 5'-flanking region. *Biochim Biophys Acta– Mole. Cell Biol. Lipids*. 2006; 1761(4):492-500.

Grayson W, Zhao F, Izadpanah R, Bunnell B, **Ma T**. Effects of hypoxia on human mesenchymal stem cell expansion and plasticity in 3D constructs. *J Cell Physiol*. 2006; 207(2):331-339.

Zhao F, Chella R, **Ma T**. Effects of shear stress on 3-D human mesenchymal stem cell construct development in a perfusion bioreactor system: experiments and hydrodynamic modeling. *Biotechnol and Bioeng*. 2006; Aug 31 [EPub].

Lannutti J, Reneker D, **Ma T**, Tomasko D, Farson D. Electrospinning for tissue engineering scaffolds. *Materials Science & Engineering C., In Print*, 2006 DOI: 0.1016/j.mesc.2006.05.019.

Zhang Y, Niu X, Brelidze TI, **Magleby KL**. Ring of negative charge in BK channels facilitates block by intracellular Mg^{2+} and polyamines through electro-statics. *J Gen Physiol*. 2006; 128(2):185-202.

Lopez D, **McLean MP**. Estrogen regulation of the scavenger receptor class B gene: anti-atherogenic or steroidogenic, is there a priority? *Mol Cell Endocrinol*. 2006; 247(1-2):22-33.

Lopez D, **McLean MP**. Activation of the rat scavenger receptor class B type I gene by PPARalpha. *Mol Cell Endocrinol*. 2006; 251(1-2):67-77.

Lagor WR, de Groh ED, **Ness GC**. Diabetes alters the occupancy of the hepatic 3-hydroxy-3-methylglutaryl-CoA reductase promoter. *J Biol Chem*. 2005; 280(44):36601-36608.

Ness GC, Holland RC. Degradation of HMG-CoA R\reductase in rat liver is cholesterol and ubiquitin independent. *FEBS Lett*. 2005; 579(14):3126-3130.

Ness GC, Holland RC, **Lopez D**. Selective compensatory induction of hepatic HMG-CoA reductase in response to inhibition of cholesterol absorption. *Exp Biol Med.* 2006; 231(5):559-565.

Schmid A, Bai G, Schmid N, Zaccolo M, Ostrowski LE, Conner GE, Fregien N, **Salathe M**. Real-time analysis of cAMP-mediated regulation of ciliary motility in single primary human airway epithelial cells. *J Cell Sci*. 2006; 119(Pt20):4176-86.

Salathe M. Regulation of mammalian ciliary beating. *Ann Rev Physiol* 2006; Aug 31 [Epub].

Alonis M, Pinnell S, **Self WT**. Bioavailability of selenium from the selenotrisulphide derivative of lipoic acid. *Photodermatol Photoimmunol Photomed.* 2006; 22(6):315-23.

Tang X, **Wang Y**. Pds1/Esp1 dependent and independent sister chromatid separation in mutants defective for protein phosphatase 2A. *Proc Natl Acad Sci U S A*. 2006; 103(44):16290-5.

Liu H, **Wang Y**. The function and regulation of budding yeast Swe1 in response to interrupted DNA synthesis. *Mol. Biol. Cell.* 2006; 17(6):2746-56.

Krotova K, Hu H, Xia SL, Belayev L, Patel JM, Block ER, **Zharikov SI**. Peptides modified by myristoylation activate eNOS in endothelial cells through Akt phosphorylation. *Brit J Pharmacol.* 2006; 148(5):732-740.

Appendix D Abbreviated Abstracts of 2006 Grant Awards

Full lay abstracts are posted on the program web site, www.floridabiomed.com.

Grant Type: New Investigator Research

ALEXANDROW, Mark

H. Lee Moffitt Cancer Center & Research Institute

Project Title: ***Functional Role of Mcm7-Rb Interactions in Ras Signaling and Tumorigenesis***

Project Summary: Several cancer types are closely associated with smoking or using tobacco products, most notably lung, hypopharyngeal, bladder, and esophageal cancers. Cancers, in general, develop from deregulation of important molecular signals in cells that control whether or not a cell is allowed to grow. One of the intracellular molecular pathways commonly altered in cancers is the Ras-Rb pathway. The Rb protein normally acts as a brake for cell growth, and Ras activation acts as the gas pedal. Preliminary results suggest that a novel complex of proteins, called the pre-replication complex, is a potential target of Ras and Rb signals. A member of this complex, Mcm7, can mimic Ras activation and block Rb when it is expressed at high levels in cells. This study addresses how Mcm7 and the Ras-Rb pathway interact to control cell growth and lead to cancer.

CAPPENDIJK, Susanne

Florida State University

Project Title: ***Acute and Long-Term Behavioral and Neurological Effects of Nicotine in the Zebra Finch***

Project Summary: In 2001, the Centers for Disease Control and Prevention (CDC) reported that there were approximately 46 million smokers in the United States; 4.1 million were adolescents. Researchers have started to show some interest in studying the effects of psychoactive drugs such as alcohol and nicotine in adolescent animals. This study will address the behavioral and biochemical effects of nicotine in the zebra finch. The National Institutes of Health recognize the zebra finch as an important non-mammalian model for neural development. Juvenile and adult animals will be subjected to single and repetitive treatments of nicotine. The acute and long-term effects of nicotine on natural behavior, and corticosterone (stress hormone) levels will be studied. Brain tissue will also be used to investigate potential neuronal damage, as well as changes in protein expression.

CHEN, Li-Mei

University of Central Florida

Project Title: ***Prostasin Protects Lung Epithelial Cell Integrity From Cigarette Smoke Induced Stress***

Project Summary: Cigarette smoking is associated with an increased incidence of airway infection and numerous diseases including lung cancer and chronic obstructive pulmonary disease (COPD). The epithelium of the lung, a layer of cells that cover the airway and in direct contact with the "outside" environment, functions as a selective barrier. Cigarette smoke damages the lung epithelium barrier and causes increased permeability by disrupting the natural "sealant" of the tissue, known as intercellular tight junctions (TJ), a complex of interacting proteins. Prostasin is a proteolytic enzyme that is necessary for maintaining TJ structure. We propose that CSE-induced reduction or loss of prostasin in the short and long term will lead to disorganization of TJs, and will promote further migration and growth of cells beyond their call of duty to repair the wound. These events will then eventually lead to the development of lung cancer. The outcome of this research will establish prostasin as a potential therapeutic agent for use in preventing and treating lung diseases resulting from cigarette smoking.

FLETCHER, Bradley

University of Florida

Project Title: ***Transposon-mediated Targeted Thrombosis of Tumor Vasculature***

Project Summary: It is well known that tobacco smoke is responsible for the overwhelming majority of lung cancers. Most lung cancer patients are diagnosed with advanced disease that is inoperable, thereby limiting treatment options to chemotherapy or radiotherapy. Unfortunately, these conventional therapies for lung cancer remain ineffective with five-year survival rates of less than 10 percent. In an attempt to improve these dismal survival rates, we describe an approach to target the blood vessels that feed and nourish the lung cancer. If these vessels could be selectively destroyed, then large portions of the tumor should die due to lack of oxygen and nutrients. The approach involves the delivery of a fusion protein with dual function. One domain of the protein recognizes the blood vessels within the tumor, while the other domain contains an effector function that destroys the vessels by promoting blood coagulation. We further aim to provide the fusion protein in the form of a gene so it can be produced endogenously.

GROBMYER, Stephen

University of Florida

Project Title: ***Metabolically Targeted Nanoshells for High Resolution In Vivo Imaging of Cancer with Finite Element Based Photoacoustic Tomography***

Project Summary: New techniques for the early diagnosis of cancer as well as new techniques for the non-invasive treatment of cancer are needed. Nanoshells are a type of multifunctional biocompatible nanoparticle that have potential as contrast agents for novel imaging of cancer, as highly specific drug delivery vehicles, and as mediators of local thermal ablation of tumors. In order for nanoshells to be effective in a living organism they must be preferentially delivered to cancer cells. This project proposes to metabolically target nanoshells to cancer cells. The metabolically targeted nanoshells will then be used to image cancer in a living organism using photoacoustic tomography. As part of this project, a photoacoustic tomography system, which utilizes a pulsed, near infrared laser with the ability to deeply and harmlessly penetrate biologic tissues will be constructed and characterized. If successful, this technique represents a new and exciting paradigm for cancer diagnostics and therapeutics.

LIU, Lin

University of South Florida

Project Title: ***Telomere Susceptibility to Cigarette Smoke-Associated Chromosomal Abnormalities in Embryos***

Project Summary: Cigarette smoking can affect female fecundity and reduce fertility. This research uses early embryo development and embryonic stem (ES) cell model systems, as well as transgenic and short-telomere mouse models to investigate whether smoking induces oxidative stress and leads to telomere shortening and dysfunction, and thus chromosomal instability, and whether telomere function plays a critical role in smoking associated defects in embryo development. Moreover, the potential role of antioxidants in preventing oxidative stress and telomere erosion, thus recovering normal embryo development, will be determined in these model systems. This project will provide new insights into how smoking causes aneuploidy or apoptosis in embryos, which can lead to pregnancy loss or birth defects. Understanding these mechanisms will help develop novel methods to prevent or treat smoking-related infertility in women, and may have general implications for understanding and prevention of other smoking-associated diseases.

LUESCH, Hendrik

University of Florida

Project Title: ***The Mode of Action of The Antitumor Agent Apratoxin A***

Project Summary: The proposed research project will comprehensively investigate the mechanism of action of the marine natural product apratoxin A, which displays potent cytotoxicity against various cancer cell lines. Apratoxin A may target a key player in cancer cell growth, which is distinct from other current targets for anticancer therapy. The identification of apratoxin A's target is a prerequisite for the potential development of apratoxin-based therapeutics and may lead to the discovery and validation of a new therapeutic target. Preliminary data showed that apratoxin A ultimately inhibits the activation of a protein called STAT3 that is critical for cancer cell growth. The cause of this desirable effect is unknown and is subject of the proposed investigation. The impact of apratoxin A on other signaling pathways critical for survival of cancer cells will be assessed using classical approaches as well as modern tools of the post-genomic era. Hypotheses derived from genomic and proteomic screens will be tested.

ROLLISON, Dana

H. Lee Moffitt Cancer Center & Research Institute

Project Title: ***Case-Control Study of Smoking and Human Papillomavirus Infection in Basal and Squamous Cell Carcinomas of the Skin***

Project Summary: Results from previous studies suggest that cigarette smoking may be associated with non-melanoma skin cancer (NMSC), the most common cancer among U.S. men and women. Infections with some types of human papillomavirus (HPV) that occur in the skin have been associated with NMSC, and preliminary data suggest that HPV may work together with smoking to promote the development of NMSC. This proposed study will investigate the interplay between smoking and HPV infection as possible causes of NMSC. Specifically, 400 NMSC cases will be recruited from the University of South Florida Dermatology Clinic (USF) and compared to 400 controls recruited from both USF and H. Lee Moffitt Cancer Center's cancer screening facility. Antibodies to the types of HPV that occur in the skin will be measured from the blood as markers of HPV infection. The goal of this research is to characterize the relationship between smoking and NMSC so that novel prevention strategies may be developed.

SMITH, Layton

Scripps Florida

Project Title: ***The Interaction Between Apelin and the Renin-Angiotensin-Aldosterone System***

Project Summary: Smoking is a key risk factor for heart disease and hypertension in particular, and leads to structural changes in the blood vessels. The renin-angiotensin-aldosterone system (RAAS) plays an integral role in maintaining blood pressure and has been implicated in the structural changes in vascular tissues often associated with hypertension. How this vascular remodeling occurs is not understood. Smoking activates the RAAS, which may explain in part the effects of smoking on the structure of blood vessels. Apelin is a newly discovered protein that acts on blood vessels to cause relaxation and thus lower blood pressure. Recent studies into how apelin works revealed that apelin could counteract the effects of the RAAS. The long-term goal of this study is to establish apelin as a counter-regulator of the RAAS and as a potential target for new drugs for the treatment of hypertension. Results from this study may provide new mechanistic insights into the molecular pathology of smoking-related arterial stiffness and hypertension.

TANG, Hengli

Florida State University

Project Title: ***Mechanism of HCV Resistance to Cyclosporine A***

Project Summary: Heavy alcohol use, tobacco smoking, and hepatitis C virus (HCV) infection are among the major risk factors for hepatocellular carcinoma (HCC), a serious form of liver cancer that costs many lives and millions of dollars in patient care every year. Cyclosporine A (Cs A) is one of the new drug candidates that have been tested in recent clinical trials with encouraging results. While both laboratory and clinical studies of Cs A-based inhibition of HCV infection are in the beginning stages, we correctly anticipated and successfully confirmed the emergence of Cs A resistant HCV strains in our lab model of HCV replication, which is called a replicon cell. Here we propose to characterize the mechanism of the drug resistance at the molecular and cellular level. Results obtained with this study will not only contribute to better understanding of HCV replication but can also provide guidance to both drug development efforts and the relevant clinical studies.

VAZQUEZ-PADRON, Roberto

University of Miami

Project Title: ***The Role of Nicotine in Smoking-Related Vascular Diseases***

Project Summary: Cigarette smoking accelerates vascular diseases, the number one cause of death in America. The diseases include macular degeneration (the most common cause of adult blindness), as well as complications of diabetes and aging (the most common cause of retinopathy, strokes, heart attacks, aneurysms, and kidney disease). Vascular diseases now claim more lives than the next seven leading causes of death (including cancer) combined, and has long been the number one killer in America. These diseases narrow the blood vessels, thus cutting blood flow to vital organs. The objective of this application is to find out how one of the main components of cigarette smoke, nicotine, contributes to increase the development of vascular diseases. Through a series of experiments that involves the application of molecular techniques to cells grown out of blood vessels, and to the actual injured blood vessels, we seek to understand how nicotine alters the biological behavior of blood vessels.

WOJCIKIEWICZ, Ewa

University of Miami

Project Title: ***Biophysical Determinants of Leukocyte Transmigration***

Project Summary: Cigarette smoking is a leading cause of heart disease, the number one killer in the United States. One of the underlying causes of heart disease is the formation of fatty streaks also referred to as lesions on the lining of blood vessels. The buildup of these fatty streaks can eventually restrict blood flow through partial blockage of the blood vessels. The extent of these lesions is greatly increased by a number of risk factors that include smoking. The long-term goal of this project is to understand the biophysical properties of the endothelial cell junctions in the presence and absence of inflammation. The contribution of the different adhesion receptors in maintaining the integrity of the endothelial junction and in how inflammation facilitates migration of the white blood cells through the junctions will be determined. The proposed studies will bring essential basic scientific knowledge, which will help in the development of better therapies against blood vessel damage exacerbated by cigarette smoke.

Grant Type: Small Business Technology Transfer

LI, Jonathan

University of Florida

Project Title: ***Eliminating Targeting Errors in Lung Cancer Radiotherapy Using Time-Resolved Volumetric Magnetic Resonance Imaging***

Project Summary: The overall aim of this project is to develop novel treatment planning software as part of a fully integrated cancer imaging, monitoring, and therapy system (Renaissance™, ViewRay Inc.) under development for curative radiation therapy of lung cancer patients. Current radiation therapy for lung cancer is complicated by patient setup uncertainties and large motions caused by natural breathing and other internal motions, which until now have not been addressed satisfactorily in radiation therapy. The Renaissance™ innovative design, combining an open split-solenoid MRI scanner and a 60Co g-ray intensity-modulated radiation therapy (IMRT) unit, allows for fast volumetric imaging simultaneous to IMRT beam delivery. No study has been performed to determine how MRI data sets can be used for heterogeneous dose calculation with acceptable degree of accuracy, especially in the thorax area. This technology must first be enabled by developing robust algorithms and approaches as proposed in this application.

MCGORON, Anthony

Florida International University

Project Title: ***A Micro-Fabricated in Vivo Bubble Oxygenator for the Treatment of Induced Severe Pulmonary Disease***

Project Summary: Oxylation, LLC, and the Florida International University Biomedical Engineering Department will establish the performance capabilities of a new and novel, in vivo, oxygen bubble catheter system for the treatment of tobacco smoke induced lung diseases. Utilizing the initial oxygenation concept created by Dr. Lary, Scientific Advisor of Oxylation, this dynamic team will utilize new technologies to accomplish three specific objectives; production and evaluation of oxygen microbubbles, implement and investigate a method for surfactant incorporation, and configure an optimal design for supplying goaled volumetric output rate of oxygen. Advances in micromachining and nanomachining, materials science, and fabrication techniques will be employed during this feasibility stage of development. The proposed oxygen bubble catheter system, (OBCS – pronounced "O-BOX"), integrates the attributes of past designs with Oxylation's novel surfactant concepts to achieve the goal of 120 ml/min of oxygen into the blood stream.

Grant Type: Team Science Program

DAVENPORT, Paul

University of Florida

Project Title: ***The Role of Nicotine in the Neural Control of Respiratory and Cardiovascular Systems***
Project Summary: Cigarette smoking is a highly addictive behavior with both short-term and long-term deleterious effects on human health. The impact of nicotine on important respiratory and cardiovascular neural control centers is the focus of the research proposed by this team of investigators. This TSP will investigate the influence of nicotine on cardiorespiratory control from the level of specific receptor subtypes within the brain to the level of human cognition and circadian behavior. Animal models in combination with human studies will provide animal-human translational research on central neural effects of nicotine on the respiratory and cardiovascular systems. The primary research approaches for this project are: 1) the role of nicotine in the modulation of respiratory sensory neural processing and reflexes and 2) the role of prenatal nicotine on the neonatal brain pathways mediating respiratory and cardiovascular neural control. The outcome of this coordinated team effort will provide new and innovative insights into the role of nicotine on central nervous system function.

Project Title: ***Oncogenic PKC iota in Smoking-Related Lung Cancer***
Project Summary: Despite our best current treatments, lung cancer survival is only 14 percent. It is estimated that over 90 percent of lung cancer is caused by smoking, the major risk factor for this disease. Chemicals in tobacco smoke cause specific mutations in the genetic material of lung cells. Studies by our TSP research team have shown that the two most common mutations caused by smoking, and which are responsible for more then 70 percent of lung cancer, have a common effect on lung cells. Specifically, we have discovered that both of these mutations activate a third gene called protein kinase C iota (PKCiota). The central theme of this proposal therefore focuses on PKCiota in smoking-related lung cancer. The overall goals of this TSP proposal are to determine how PKCiota causes lung cancer and how it controls cancer growth and spread, and to evaluate a new drug recently discovered by our group that inhibits PKCiota.

FIELDS, Alan

Mayo Clinic

LEE, David

University of Miami

Project Title: ***Reducing the Burden of Tobacco-Associated Cancers in Florida***
Project Summary: More than 582,000 Floridians currently suffer from tobacco-associated health problems such as cancer and heart and lung diseases. Counties in northeast Florida were found to have high rates of new cases of tobacco-related cancers, and counties in the panhandle were found to have high rates of tobacco-related cancer deaths. This proposal lays the groundwork for testing three levels of interventions to reduce tobacco-associated cancer risk in these counties by: 1) reducing tobacco use (primary prevention); 2) increasing early detection of cancer (secondary prevention); and 3) ensuring access to state-of-the-art treatment (tertiary prevention). The first aim is to identify areas of Florida in greatest need of primary prevention by mapping county-level smoking prevalence data from the Behavioral Risk Factor Surveillance System and the Florida Youth Tobacco Survey. The second is to identify areas of Florida in the greatest need of secondary and tertiary prevention by using spatial analysis methods that will illustrate tobacco-associated cancer clusters. The third and last aim is to identify areas of Florida in need of secondary and tertiary prevention by using data from Florida Cancer Data System and from the Florida Agency for Health Care Administration to map late-stage presentation of tobacco-associated cancers and to evaluate access to state-of-the-art medical care for tobacco-related cancers. All projects will be supported by a Biostatistics and Data Management Core, and an Outreach, Education and Dissemination Core.

Appendix E National Institutes of Health, Funding by State

2005-2006 Funding by State[9]

States are listed in order of total funding received in 2006.

	2006							2005	
State	2005 Population Estimate	Pop Rank	$ Per Capita	Per Capita Rank	Funding 2006	Rank	% of Total Funding	Funding 2005	Rank
California	36,132,147	1	84.36	11	3,048,138,519	1	15.11%	3,135,216,412	1
Massachusetts	6,398,743	13	335.9	1	2,149,369,222	2	10.65%	2,190,122,025	2
New York	19,254,630	3	95.91	10	1,846,780,769	3	9.15%	1,942,072,401	3
Pennsylvania	12,429,616	6	107.28	7	1,333,388,400	4	6.61%	1,411,362,641	4
Texas	22,859,968	2	45.54	26	1,041,045,029	5	5.16%	1,101,332,516	5
Maryland	5,600,388	19	172.3	3	964,957,683	6	4.78%	1,007,771,813	6
North Carolina	8,683,242	11	104.24	8	905,135,143	7	4.49%	902,740,214	7
Washington	6,287,759	14	127.71	5	803,033,656	8	3.98%	765,429,351	8
Illinois	12,763,371	5	53.15	21	678,357,778	9	3.36%	696,401,965	9
Ohio	11,464,042	7	53.49	22	613,183,796	10	3.04%	633,899,896	10
Michigan	10,120,860	8	52.93	23	535,678,937	11	2.66%	545,620,905	11
Missouri	5,800,310	18	79.38	12	460,424,407	12	2.28%	490,241,305	12
Connecticut	3,510,297	29	124.79	4	438,035,882	13	2.17%	449,285,014	13
Tennessee	5,962,959	16	68.04	16	405,745,744	14	2.01%	421,184,016	14
Minnesota	5,132,799	21	76.24	13	391,328,715	15	1.94%	401,700,381	15
Wisconsin	5,536,201	20	65.15	17	360,689,308	16	1.79%	358,748,939	18
Georgia	9,072,576	9	38.81	30	352,122,831	17	1.75%	365,758,450	17
Florida	**17,789,864**	**4**	**18.61**	**45**	**331,128,265**	**18**	**1.64%**	**367,266,181**	**16**
Colorado	4,665,177	22	63.09	18	294,328,406	19	1.46%	323,913,381	19
Oregon	3,641,056	27	72.08	14	262,452,372	20	1.30%	265,415,014	21

Section 215.5602, *Florida Statutes* — Appendix F
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 Secretary of Health 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 Secretary of Health, 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 Secretary of Health, 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 Secretary of Health, 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 oand statutory citation of this section, which is scheduled to expire January 1, 2011.

(14) The Legislature shall review the perormance, 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 appropriat 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.

Endnotes

[1] The 2006 Bankhead-Coley Cancer Research Program Annual Report is available at http://www.floridabiomed.com.

[2] U.S. Centers for Disease Control and Prevention, Behavioral Risk Factor Surveillance System, 2005. Available at http://apps.nccd.cdc.gov/brfss/display.asp?yr=2005&cat=TU&qkey=4396&state=FL, accessed on 10/20/2006.

[3] s. 215.5602, *F.S. – James and Esther King Biomedical Research Program,* available in Appendix F.

[4] Engle v. Liggett Group, Inc., SC03-1856.

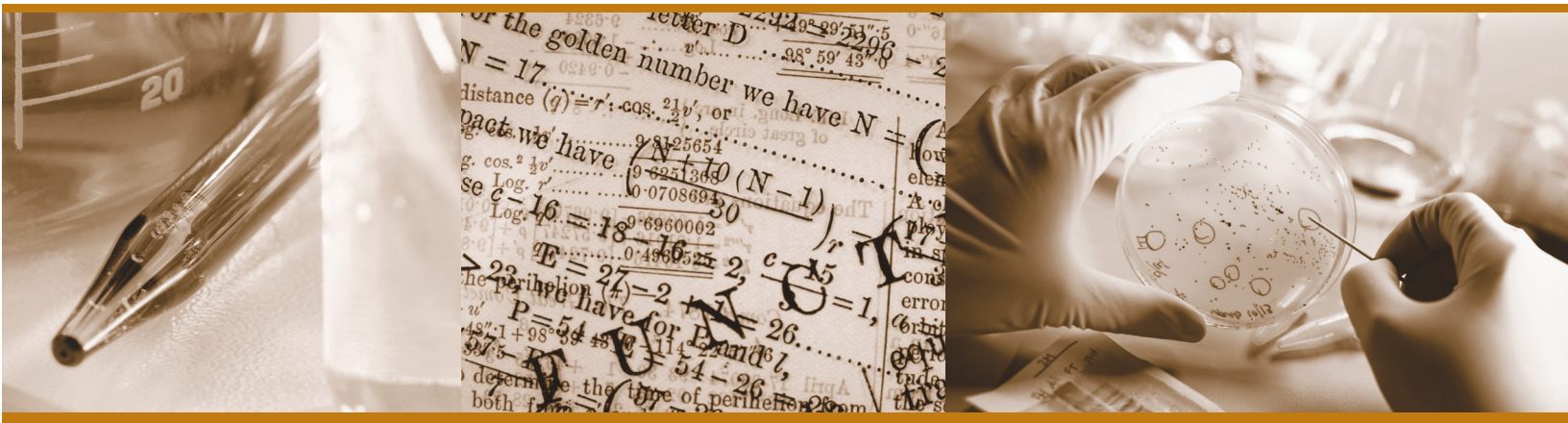
[5] Moses H, Dorse, ER., Matheson JD, Their SO. Financial Anatomy of Biomedical Research. *JAMA*, September 21, 2005; 294; 1333-1342.

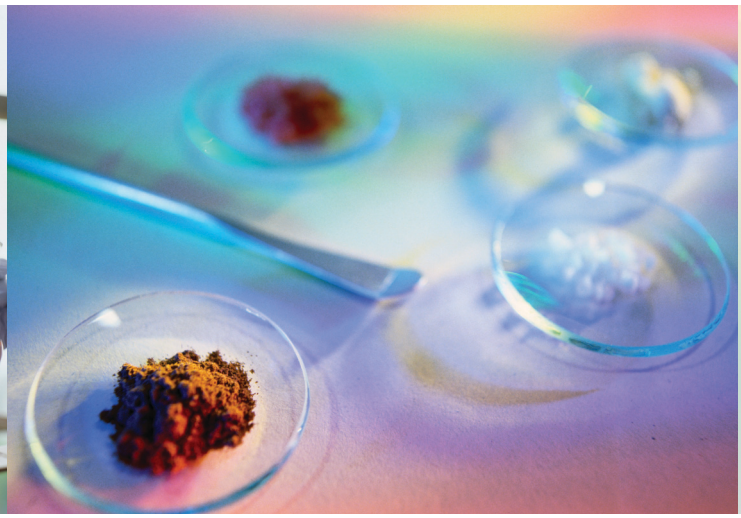
[6] Welker ME, Cox AR. A Report on Research Activities at Research Universities, *Research Management Review, The Journal of the National Council of University Research Administrators.* Volume 15, Number 1 Winter/Spring 2006.

[7] American Society for Biochemistry and Molecular Biology, Letter to NIH Director Zerhouni lays out ASBMB Concerns regarding Grant Funding, Poor Success Rates, available for download at http?//www.asbmb.org/ASBMB/site.nsf/web/791851D5677489B8852571B10067DFDF?OpenDocument, accessed on 12/9/2006.

[8] NIH Office of Extramural Research, NIH Investment in Extramural Research and Training Programs, available for download at http://grants.nih.gov/grants/news.htm, accessed on 10/25/2006.

[9] Sources: Population Estimates - http://quickfacts. census.gov/qfd/index.html, accessed on 09/18/2006. NIH Funding Data - http://grants1.nih.gov/grants/award/state/state.htm, 2006 data accessed on 10/20/2006, 2005 data accessed on 10/20/2005.





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