# Creating hope

## at home and abroad

2008 ANNUAL REPORT

SFBR

Southwest Foundation for Biomedical Research

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# Creating hope at home and abroad

2008 ANNUAL REPORT

# *Mission Statement*

*The Southwest Foundation for Biomedical Research is dedicated to improving the health of our global community through innovative biomedical research.*

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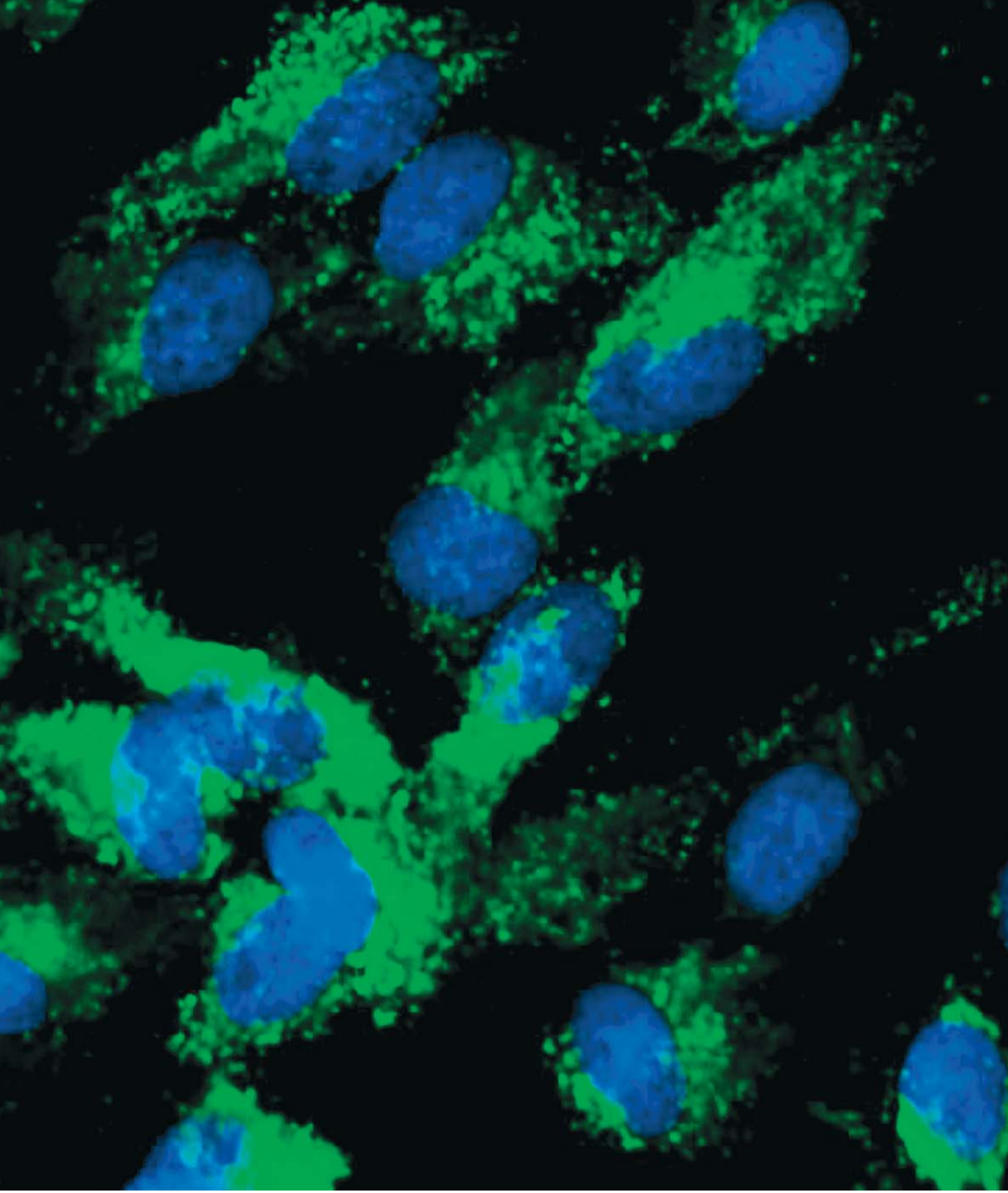


*Cultured endothelial cells derived from a baboon artery.*

# *Letter from the President*

My first months as president and CEO of the Southwest Foundation for Biomedical Research have been very exciting, and I am honored to be working with such an outstanding group of researchers, board members, management staff, and donors. Having worked with several independent biomedical research institutes over the last 26 years, I can say unequivocally that the Foundation is among the premier scientific organizations in the United States.

How do we judge our success? In my view, a biomedical research institution can be evaluated by two broad criteria:

- First, by the quality of scientific inquiry undertaken by its faculty as measured by such factors as publications in high-impact journals, the level of grant support from the National Institutes of Health and other funding agencies, and discoveries actually transferred to commercial entities for the public benefit.
- And second, by the quality of research conducted by third parties that is enabled, in part, by the intellectual leadership of the organization and the scientific resources that the organization can bring to bear.

By these measures, the Foundation is performing at an extremely high level. It is recognized throughout the world for the quality and diversity of its research activities. As recorded in the most prestigious peer-reviewed journals, the scientific endeavors conducted here in such areas as viral infections, parasitic diseases, the inherited underpinnings of a variety of illnesses, the development of animal models of human diseases, and investigation into preventive and therapeutic strategies against bioterrorism, mark the Foundation as a global scientific leader.

Right here, and right now, new approaches are being explored in addressing tuberculosis, pre-eclampsia, heart disease, diabetes, AIDS, cystinosis, Chagas disease, malaria, hepatitis C, and a wide range of other illnesses that kill and debilitate millions of people every year.

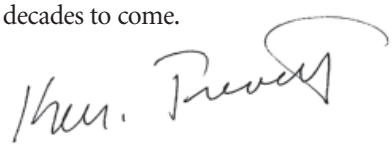
Some of this work will have a real impact on medical care in just a few years. The most obvious examples of near-term technology development are the Foundation's steroid chemistry discoveries now being commercialized by Evestra™ to address many women's health issues. Other efforts may take a generation to spawn changes in medical care. But of special note, in the continuum between laboratory discovery and improved health care, the Southwest Foundation is recognized internationally as a critical player.

The second criterion, enabling good research by others, is perhaps too little appreciated. Through the generosity of our friends in San Antonio and beyond, and the vision of our scientific leaders and faculty, we have brought together a truly powerful combination of research resources from the AT&T Genomics Computing Center, to the nonhuman primate colonies, to human study populations, to highly sophisticated biocontainment laboratories. These resources are available to our own scientists and to others who come here to work, or who utilize animals and animal tissue from our colonies, or who take advantage of our genetic analysis software, called SOLAR, to unravel highly complex biologic and pathologic questions.

Similarly, our scientists seed the intellectual fields around them by training postdoctoral fellows, hosting visiting scientists, or traveling across this country and around the world sharing their knowledge and skills.

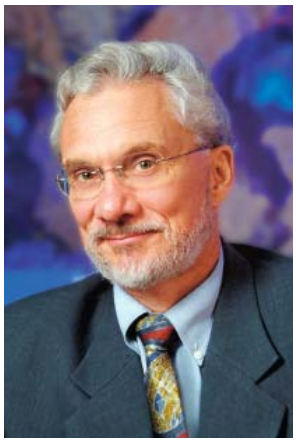
There is no better time to be in the biological sciences – or to be affiliated with the Foundation – as a researcher, trustee, member of management, or donor. We have the opportunity for bold initiatives and have the benefit of a great breadth of spirit.

The Foundation represents hope and continues to fulfill hope. With your ongoing help, we will do so for decades to come.



**Kenneth P. Trevett**
*President and CEO*

# *Letter from the Chief Scientific Officer*



The Foundation capitalized on its scientific strengths in genetics, virology, and nonhuman primate research in 2008 to contribute to the advancement of science in ways that will improve the health of people in the United States and throughout the world. SFBR's investigators contributed 127 publications to the international scientific literature. Some of these important papers are the bases of feature stories in this report. Scientific achievements documented in the papers include –

- Discovery of the chromosomal locations of genes with profound effects on susceptibility to intestinal worm infections, suggesting the promise of developing vaccines (*Journal of Infectious Diseases* 197(1): 66-71, and *Journal of Infectious Diseases* 197(8): 1198-1203).
- Advances in biodefense, including a new method for the detection of the botulinum neurotoxin (*Analytical Chemistry* 80(22): 8583-8591) and an experimental vaccine that protects animals from deadly Ebola virus and may provide the key for developing the first human vaccine for this virus (*Virology* 383: 12-21).
- The finding that baboons develop osteoporosis just as do humans and represent a new model for research on the prevention of this disease (*Journal of Medical Primatology* 37(3): 146-153).
- Identification of a new cancer model, the newborn opossum, which may provide a novel strategy for understanding human cancer metastasis and for treating virtually all types of tumors (*International Journal of Clinical and Experimental Pathology* 2(3): 286-299).

In addition to these cutting-edge discoveries, SFBR scientists in 2008 received significant new grant awards that will support new avenues of research aimed at improving human health. It is a profound tribute to the caliber and perseverance of our 32 principal investigators that, despite increased competition for flat funding from the National Institutes of Health from 2004 to 2008, federal grants and contracts to the Foundation increased by 15.4 percent over that same period of time, and they increased by 6.4 percent from 2007 to 2008, reaching a record high of $37 million.

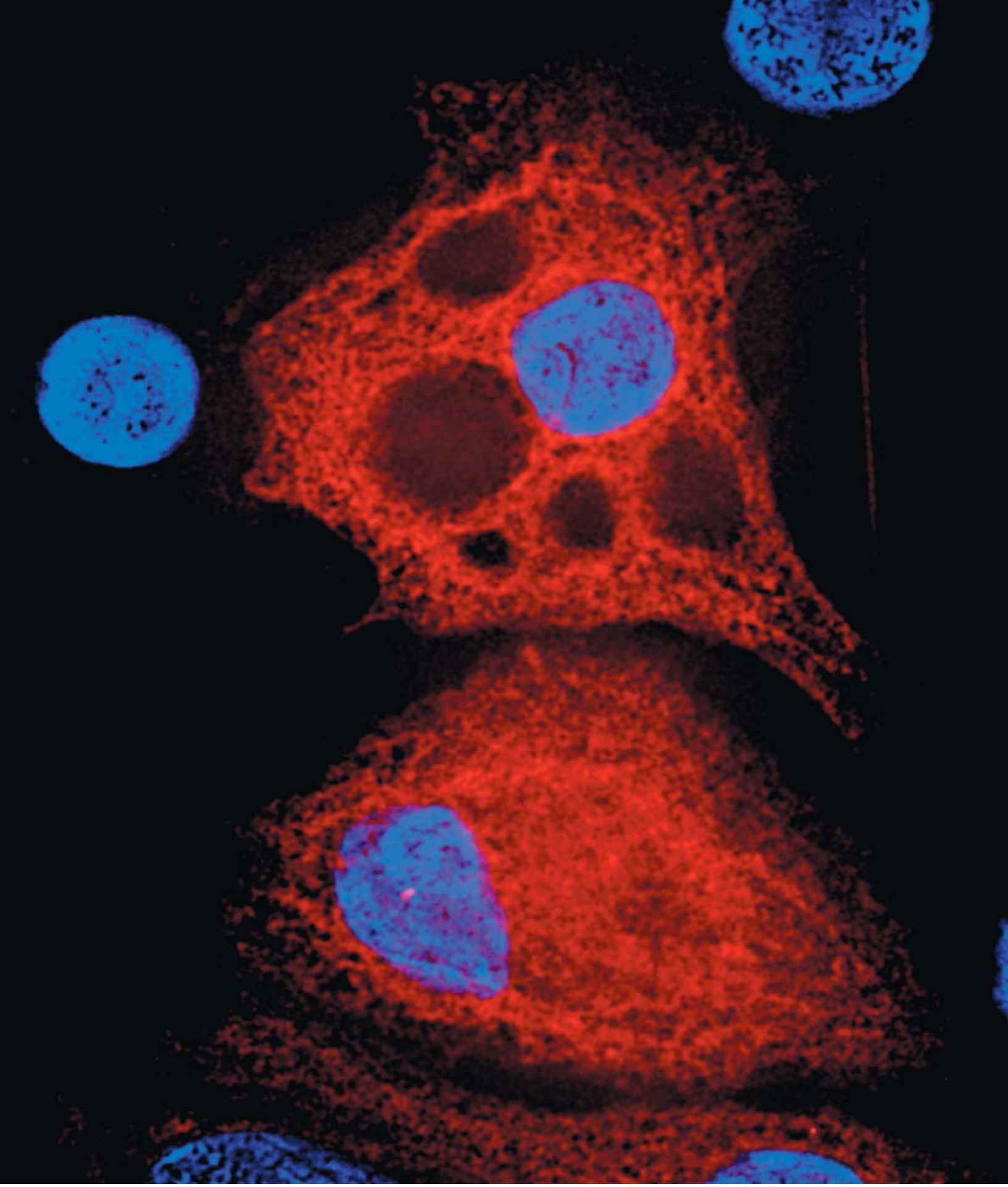
A five-year $18.8 million federal research grant – the largest in SFBR's history – will allow our scientists to embark on several ground-breaking and unique studies of cardiovascular disease, the nation's No. 1 killer.

The studies include (1) how cells in the lining of different individuals' arteries vary in their response to disease-causing stimulants and a search for genes that regulate those cellular responses; (2) an investigation into genetic variation among individuals in the body's production and circulation of a type of adult stem cell produced by bone marrow that plays a long-term protective role against the buildup of dangerous fatty plaques in the arteries; (3) the health effects of the high-fat, high-cholesterol diet so common in Western societies today; and (4) the examination of entire networks of genes that influence physiological risk factors, such as blood cholesterol levels or obesity, versus searching for one disease-influencing gene at a time. The results of this study will provide important answers in our constant effort to translate the latest basic science findings into practical drugs and other therapies that directly improve the lives of people everywhere.

I am excited by the opportunity to work with Kenneth P. Trevett, SFBR's new president, who has vast experience in the management of research organizations. His expertise, combined with our scientists' prolific publication in high-impact journals, and SFBR's strong board of trustees and donor base, puts us in an outstanding position to fulfill our mission to improve the health of our global community through innovative biomedical research.

Sincerely,

**John L. VandeBerg, Ph.D.**
*Chief Scientific Officer*



*Immunological stain of hepatitis virus in liver cells.*

# SFBR Scientists Uncover Genetic Roots of Parasitic Infections

Each June and December, Southwest Foundation for Biomedical Research geneticist Sarah Williams-Blangero, Ph.D., trades the safety and comfort of her San Antonio laboratory for a hair-raising drive toward Mount Everest in the Himalayan mountains of Nepal.

But Williams-Blangero does not brave eight hours down a narrow mountain highway full of hairpin turns in order to scale the world's tallest peak.

The chair of the Department of Genetics at the Foundation, she travels on a scientific quest, seeking the genetic roots of parasitic infections that plague a quarter of the world's population.

Her long and tiring journey brings hope to a medically underserved region of the world: Jiri, a cluster of mountain villages in eastern Nepal where 2,600 people from one extended family live in mud brick houses and farm on rocky hillsides.

Williams-Blangero has been making this trek once or twice a year since she was in graduate school. First, it was for a thesis on how marriage patterns affect biological variation within a population. Since the early 1990s, she has involved the Jirel people in an SFBR-led project to study predisposition to helminthic infections that plague people in underdeveloped regions of the world. It is a study that now is bearing fruit. In the last two years, Williams-Blangero and her team have made significant progress in explaining genetic susceptibility to these infections, identifying regions in the genome where the culprit genes lie.

Two major papers were published in 2008 in the *Journal of Infectious Diseases* that narrow the search for these genes.

*Study participants are recruited during house to house visits in Jirel villages such as the one shown here.*

*A study participant documents his consent to participate in the study during an interview on the porch of his home.*

The SFBR-led team isolated six regions on four different chromosomes that appear to influence susceptibility to roundworm infections. Three of those regions, on chromosomes 8, 11, and 13, gave off strong signals of involvement, while three other potential regions also were identified.

A second publication reported the first genome-wide linkage scan for whipworm susceptibility, identifying four gene regions that may be involved. Two regions, on chromosomes 9 and 18, have high probability of involvement, and the evidence also suggested two other regions may contain genes that round out the picture of inherited risk.

Work now continues to identify the specific genes that determine who is susceptible to chronic worm infections.

While treatments are available already for these conditions, researchers hope their genetic study will lead to better care. SFBR scientists also think the genes could be important in explaining vulnerability to other parasitic diseases that afflict people throughout the world.

More commonly known as hookworms, whipworms and roundworms, helminth larvae thrive in soil where sanitation is poor and people don't have access to treatment or preventive care. People are continuously exposed through contaminated food or through contact with the soil, because some of the species can burrow through the skin.

Chronic exposure has lifelong health consequences. Continual worm infestations can stunt physical growth and cognitive development and make people susceptible to other infections. Women and adolescent girls are more prone to anemia, and severe worm loads can cause intestinal blockages and death in children.

The World Health Organization estimates that almost 2 billion people have chronic intestinal worm infections. But even in regions where people share the same environment, some members of a population are more prone to infections than others. Estimates are that in any infected group, about 10 to 20 percent of the human population harbors 80 to 90 percent of the worm burden. That suggests an underlying genetic susceptibility, a puzzle

*The older members of the community are important sources of information about the relationships between different families in the Jirel population.*

that Williams-Blangero and her team have been working to solve for more than 15 years.

"What makes that 10 to 20 percent different?" she said. "That is what we want to know."

The Jirel people have lived in this mountainous region of eastern Nepal for generations. They have a unique language and culture and marry within the population, seldom moving far from their roots. Such people are treasure troves for genetic scientists who want to investigate the heritable nature of complex diseases involving more than one gene.

Using relationships she built through her first family study of the Jirels in the mid-1980s, Williams-Blangero returned to the region in 1995 after receiving her first round of federal funding to investigate the questions surrounding parasitic worm infections.

Most of the work has been supported by grants from the National Institutes of Health. Williams-Blangero's first grant to support the research was awarded in 1995 and totaled $750,000. Since then, Williams-Blangero has written grants that have resulted in an additional $8.5 million of support awarded to SFBR for the study of susceptibility to helminthic infections. The Founders' Council and the Southwest Foundation Forum also have provided critical support over the years.

The project has brought added benefits to the Jirel people. The researchers brought along physicians, clinical staff, and treatments for the people who were infected with worms. The project's clinic is staffed by Nepalese medical professionals who provide routine medical care to the villagers. Twelve Jirels now work for the research project and clinic, channeling valuable resources into the struggling region.

"The study has had a real practical benefit for the people there. In order to study the genetics of helminthic

infections, you have to treat the people," Williams-Blangero said. "This really has become their primary source of medical care."

The project has involved other scientists over the years, including SFBR scientist John Blangero, Ph.D., who helped set up the study site and has performed computer analyses of the data. Chief Scientific Officer John L. VandeBerg, Ph.D., generated the molecular data and collaborated in the genetic analyses.

Just about all of the Jirels residing in the seven sampled villages are enrolled in the study, which has accumulated a wealth of genomic data that has been tapped by other researchers. Bradford Towne, Ph.D., of Wright State University in Dayton, Ohio, collaborated with SFBR to study genetic components of childhood growth in the Jirel people; and Susan Santangelo, Sc.D., of Harvard University looked at genetic factors influencing risk factors for psychiatric diseases.

SFBR soon will start a new collaboration with Wright State University to look at the genetics of dental characteristics in the Jirel people.

"There are few populations in the world so well-characterized genetically," Williams-Blangero said. "The potential for this pedigree to be used for any genetic study is huge."

The Jirel project represents the genetics department's focus on the overall mission of Southwest Foundation for Biomedical Research, Williams-Blangero said. "There is a real commitment to understanding international health problems. The Foundation's mission is to improve the health of our global community, and the department really does have a strong focus on that."

Since beginning her journeys to Nepal in 1985, Williams-Blangero has watched a generation of Jirel children grow and thrive with the help of the medical care her project brought to the isolated region. Research scientists have developed an excellent rapport with the participants and staff over the many years of the study.

"Our staff usually gather flowers from the surrounding area and are standing there with bouquets when we arrive," Williams-Blangero said. "Working in Jiri has been a wonderful experience, and I am very grateful to all the Jirels who have generously participated in our studies." ■

*Children are important participants in the genetic studies of worm infections. Individuals three years of age and older are recruited into the research project.*

# Drug Trial Shows Promise for Treating Hepatitis C And for a New Technology to Fight Other Diseases

Recent evaluation in chimpanzees of a new antiviral therapy for hepatitis C developed by the Danish firm Santaris Pharma has yielded promising results for those infected with the virus and, at the same time, has the added bonus of lowering blood cholesterol levels. More important is the technology itself, which could be used to target genes involved in cancer, HIV, and inflammatory diseases. "Now that we know it works, the possibilities seem limitless," said Robert E. Lanford, Ph.D., a scientist with SFBR's Department of Virology and Immunology.

The treatment shuts down a liver function that hepatitis C virus (HCV) needs in order to replicate. That same liver function also regulates cholesterol levels in the blood. So while clearing the body of HCV, this new therapy also lowers blood cholesterol dramatically, said Lanford, who is one of the world's leading experts on HCV and other liver diseases.

Hepatitis C infection is the No. 1 reason for liver transplants and liver cancer.

Approximately 3.2 million people in the United States are believed to be chronically infected with hepatitis C. Worldwide, about 170 million people are infected, and 4 percent of the adult population in the United States has the virus.

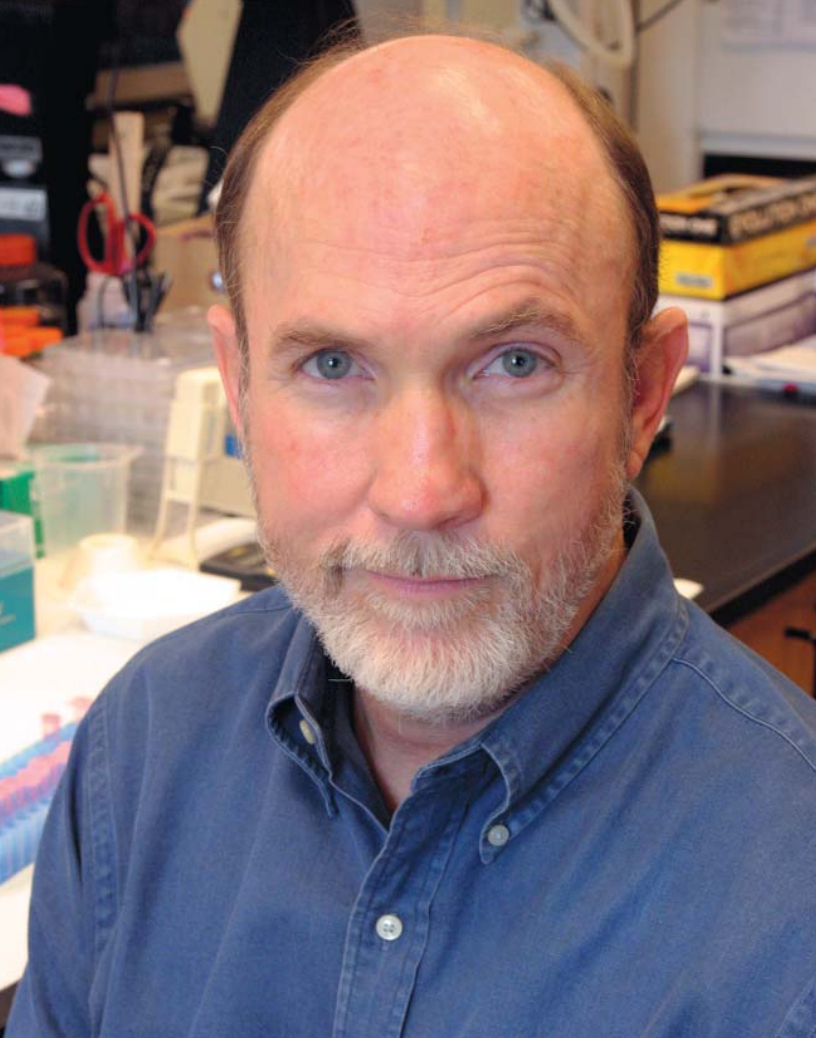
For years, hepatitis C has been called the "silent epidemic" because a chronic infection can persist for decades before causing symptoms, such as cirrhosis of the liver. Cirrhosis itself can be fatal, with scarring that impairs liver function and blood circulation, and can lead to liver failure. Hepatitis C infection is already the leading cause of liver transplants in this country, but now the United States is also experiencing an increase in the rate of HCV-related liver cancer. It has become the most rapidly increasing cause of death from cancer in the United States.

Lanford detailed the novel therapy his team tested in collaboration with Santaris in an article that has been submitted for publication in a leading scientific journal, and in a presentation in October 2009 in Nice, France, at the International Symposium on HCV and Related Viruses.

The therapy was one of 10 HCV antiviral compounds that Lanford's team tested for seven pharmaceutical companies in 2008 using the chimpanzee model of HCV infection at Southwest National Primate Research Center (SNPRC). In addition to the Santaris therapy, most other therapies showed promising results; but some did not.

"The ones that fail are important as well, because our testing means humans will not be exposed to ineffective drugs during clinical trials," Lanford said. "Companies often reconfigure their drug and come back to us with something highly potent. Several of the compounds that we tested this year have already progressed to human clinical trials. Five years ago, we were lucky to see drugs that suppressed the virus by more than 10-fold, but now we see drugs that can drop the level of virus by 10,000-fold in a few days. We had major presentations at international scientific meetings in 2008 on our studies with Abbott Labs, Idenix Pharmaceuticals, Anadys Pharmaceuticals, Massachusetts Biologic Laboratory, and Santaris."

Because HCV mutates rapidly, a combination of drugs, referred to as a cocktail, typically is required to suppress the emergence of antiviral-resistant viruses. The "holy grail" in HCV therapy research, said Lanford, has been to look for alternatives to the only U.S. Food and Drug Administration-approved therapy for HCV, a 48-week regimen of the harsh cocktail of pegylated interferon-alpha and ribavirin. The treatment makes patients extremely sick with severe flu-like symptoms and also causes depression, among other debilitating side effects. The cure rate from that drug cocktail is less than 50 percent. The most common approach for the newer therapies is to design a drug that directly attacks part of the virus. These drugs are generally referred to as STAT-C for "specifically targeted antiviral therapy for HCV" and include drugs known as protease inhibitors, polymerase inhibitors, nucleoside analogues, and NS5A inhibitors. The concept here is to have a cocktail of at least three drugs that attack different viral functions to prevent resistance.



*Robert E. Lanford, Ph.D.*

The therapy tested for Santaris, a synthetic nucleic acid or DNA, takes a different approach. "Viruses depend on many of the functions within the host to make new viruses," Lanford said. "Unlike bacteria, viruses cannot autonomously replicate in a test tube. They have to be inside of a cell, and they use many of the functions of that cell in order to replicate." The dependence of viruses on the host can be their weakness. "The problem is that most of the host functions are essential, and inhibition of the function will have adverse consequences," Lanford said. "The body doesn't make things for viruses to replicate with. Viruses co-opt them. They hijack them and use them for their own purposes."

HCV is dependent on a small RNA molecule in the liver called a microRNA, an important regulator of cellular functions. HCV cannot replicate without attaching to a specific microRNA in liver cells, identified as miR122, Lanford said. If the virus cannot replicate, it disappears from the body.

The concept of blocking miR122 to inhibit HCV replication had worked in tissue culture, but to find out if it worked in a living organism, Lanford's team needed to test it in the chimpanzee, an animal physically similar to humans and the only animal other than humans that can be infected with HCV. Testing in chimpanzees provides essential data on how well the body "takes up" a drug therapy, how well the drug reaches the liver, and how long before the drug disappears. This determines the dose and how often people need to take a medication. Tests with chimpanzees also reveal how potent a drug is, or how quickly it reduces the level of the virus in the blood.

For the new drug, Lanford's team needed to answer the question of whether it would truly suppress the level of the virus, or whether the virus would learn to replicate without miR122. The testing represented advances for two reasons. First, it proved the feasibility of inhibiting the virus by blocking miR122 and that the virus could not develop resistance to the drug. Because the drug does not directly bind the virus, the virus cannot mutate to prevent binding. The second advance was the proof of concept for the technology called "locked nucleic acid" or LNA. The drug not only targeted the liver well, but it kept working for months after the last dose. It was very stable in the body and actually suppressed the virus long enough for the researchers to see the liver become healthier.

Since microRNAs regulate essential host functions, such as production of proteins that the body needs, shutting one down can have negative consequences for the person's health. However, in extensive testing, Lanford's team observed no toxic effects. In this case, the LNA against miR122 had an additional positive consequence.

"When we bind miR122, not only do we knock out viral replication, but we knock out other things that miR122 regulates," Lanford said. "One of the things miR122 does is regulate the production of cholesterol by the liver. So when we inhibited miR122, we knocked down cholesterol levels in the blood by as much as 45 percent. We lowered cholesterol better than the leading cholesterol medications that are on the market."

Probably the most important aspect of this work is that LNAs can be made to directly target any nucleic acid sequence. Thus, this same technology should work for genes involved in many disorders, including cancer, HIV, and inflammatory diseases. "Clearly, we will be hearing more about LNAs in the news, and hopefully we will be doing more of the testing here at SFBR and SNPRC," Lanford said. ■

# Pioneering Geneticist Jean MacCluer Retires, Founded the San Antonio Family Heart Study

Jean MacCluer, Ph.D., joined the staff at Southwest Foundation for Biomedical Research in 1981 with the ambitious goal of implementing exciting new computing technologies in the field of genetics research.

There was just one problem. There were no computers. Not for scientists, at least.

MacCluer laughs now about that inauspicious start, when she had to borrow computing time from the SFBR business office and run her first data sets on a circa 1970s Hewlett-Packard machine that was more accustomed to processing simple payroll records.

As she moves into retirement 28 years later, MacCluer, 72, is pleased to observe that there is no longer a shortage of computers. Scientists at the Foundation have access to a building full of them at the AT&T Genomics Computing Center, all capable of running in tandem to push out in days the complex genetic analyses that once took months or years to finish.

That hardware build-up was driven by the scientific calling that MacCluer answered: detailed studies of extended families to hunt for genes that make some people more susceptible to life-threatening heart disease, diabetes, and kidney failure.

Her tenure helped shape the Foundation's focus on investigating the genetic roots of complex but common diseases involving more than one gene. It is work that has offered hope to millions of people who struggle with potentially fatal diseases that affect their daily lives.

MacCluer is probably best known for starting the San Antonio Family Heart Study, an inquiry that began in 1991 and still involves 1,400 individuals from 40 extended Mexican-American families in an ongoing search for genes that influence risk factors for cardiac disease. That work grew in scope, stimulating similar family-based studies of minority health issues and

drawing MacCluer and the Foundation into research with American Indian and Alaskan Eskimo populations.

MacCluer also made a lasting mark on the field of genetics research by inaugurating a biennial Genetic Analysis Workshop that has grown into an international enterprise for testing new methodologies.

"Certainly the Department of Genetics wouldn't be anything like it is if Jean hadn't come here," said SFBR Chief Scientific Officer John L. VandeBerg, Ph.D., who made MacCluer his first hire after starting the department in 1980. "She's more than left a mark on it; she helped me develop the department into what it is, and it was every bit as much her vision as it was mine."

"A lot of the strengths we have today really grew out of her initial collaborations," said Sarah Williams-Blangero, Ph.D., chair of genetics at SFBR. "She was a pioneer in the application of computer methods to genetics questions, which also has become a major strength of the department as a whole."

MacCluer and her partner, Bennett Dyke, Ph.D., left faculty positions at the Pennsylvania State University to join SFBR at a key time, when VandeBerg, new to the Foundation himself, was establishing a full-fledged genetics department.

Dyke, who came with an expertise in computer applications, joined MacCluer in helping VandeBerg set the tone and direction of the department. "I had a vision, and they had ideas and experience that helped make that vision become reality," VandeBerg said. "It was a wonderful collaboration."

The Foundation already was home to a research baboon colony, which became the first focus of MacCluer's work into genetic and dietary factors influencing coronary artery disease. But even at the earliest days of those studies, MacCluer already was thinking about how to look at the same issues in people. When interviewing for the job at the Foundation in 1980, she met Michael Stern, M.D., from the University of Texas Health Science Center in San Antonio, who had begun an epidemiological study of coronary risk factors in Mexican Americans. They talked then about collaborating in the future to home in on the genes that made some families more prone than others to heart problems.

A decade later, that idea bore fruit. In 1991, MacCluer secured a $178,000 seed grant from Corpus Christi benefactors Virginia Joslin and Ruth Campbell to begin collecting data and enrolling San Antonio families in her study. With those first findings, the Foundation landed its initial round of federal funding – $9 million from the National Institutes of Health's National Heart, Lung, and Blood Institute.

In the last 18 years, the project and its offshoots have drawn $65 million total grant money and enabled scientists to publish more than 200 papers. Researchers have discovered two novel genes influencing cholesterol metabolism and inflammation and have narrowed the hunt for as many as 40 others to specific regions of the genome.

The genetic data from 1,400 willing San Antonio volunteers also has proved to be an invaluable asset to scientists interested in complex issues beyond cardiovascular disease. Ongoing studies are using the family pedigrees to study the determinants of brain structure and function and to understand normal variation in a single gene which may cause a devastating metabolic storage disorder, cystinosis, when in a mutated form.

**I think mostly what I am is a facilitator. I saw opportunities, and I pursued them. I don't feel retired yet. I may have committed myself to too many things before I retired.**

*– Jean MacCluer, Ph.D.*

As collaborators on the San Antonio Family Heart Study began making discoveries, their findings naturally gave rise to questions about genetic issues in other minority populations, spawning a web of studies that utilize the Foundation's scientists and computing resources.

MacCluer became involved in the Strong Heart Study, headquartered at the University of Oklahoma, which is looking at heart disease risk factors among 13 American Indian tribes. In 2000, the question extended to Alaskan Eskimos through the GOCADAN study, an acronym for Genetics of Coronary Artery Disease in Alaska Natives. She also is participating in a study on the genetic underpinnings of kidney disease among Zuni Indians.

"I think mostly what I am is a facilitator," MacCluer said. "I saw opportunities, and I pursued them."

Her other major career accomplishment really began with a spirited argument between two genetic scientists at the 1981 American Society of Human Genetics meeting over whose approach to solving a problem was better.

By the end of the meeting, organizers put MacCluer in charge of running a contest the following year. She was to generate simulated data about a genetic problem and let contestants apply their methodologies to see who was better at solving it.

"I came back just petrified; I'd been here only a couple of months, and we didn't even have our own computing facilities yet," MacCluer recalled. She was able to use business office computers at the Foundation, and generate data sets that drew seven entries for the first contest in 1982.

The participants and organizers were enthusiastic, and as with most other projects in her career, her contest grew. The Genetic Analysis Workshop has become a biennial event; it now draws 300 or more entries and is large enough to merit its own advisory board that prepares for the exercise. Participants present their findings at the workshop, and results are published in a scholarly journal.

"It is a way of developing methodology and also a big training ground for young scientists," MacCluer said.

The Genetic Analysis Workshops have had a huge influence on the field of statistical genetics, said John Blangero, Ph.D., an SFBR scientist who began his career as a post-doctoral fellow in MacCluer's laboratory.

"Jean was a pioneer in the use of computers in studying human genetics, and the Genetic Analysis Workshop was what was used to develop these tools," John Blangero said. "It was absolutely critical to the development of the field."

*Bennet Dyke, Ph.D., and Jean MacCluer, Ph.D., shortly after arriving at SFBR.*

MacCluer officially retired from SFBR December 31, 2008, but still maintains an office at the Foundation and remains a consultant to the studies she started. John Blangero now is the principal investigator of the San Antonio Family Heart Study. Anthony Comuzzie, Ph.D., is the Foundation's lead investigator in the GOCADAN study; and Shelley Cole, Ph.D., is taking over MacCluer's position in the Strong Heart Study. Laura Almasy, Ph.D., will lead the Genetic Analysis Workshop.

After a 40-year career and more than 200 published papers, MacCluer now has a new project to undertake: learning how to relax. She still is editing and writing papers, flying to meetings to speak on the Foundation's behalf, and participating in professional committees.

"I don't feel retired yet," she said. "I may have committed myself to too many things before I retired, thinking I would be bored. Now the pace is slower, but maybe not slow enough."

She and Dyke, who retired from the Foundation five years ago, recently built a new house on three acres of land in Northwest San Antonio and are settling in. Her 100-year-old mother lives with them, and MacCluer is hoping to get a little domestic.

"I love to cook, and I would like to try to do some gardening," she said. "It's something I haven't done for the last 30 years." ■

# SFBR Research Offers Hope For Surviving the Unthinkable

Even before the anthrax incidents that followed the September 2001 terrorist attacks on the United States, SFBR scientists were working on the front lines of the battle to make people at home and abroad less vulnerable to bioterrorism. In 2008, SFBR scientists made significant advances in the development of vaccines, a new animal model for research, and a search for potential new uses for drugs already approved and on the market.

"We are working hard to protect people from these threats to public safety," said SFBR's Ricardo Carrion Jr., Ph.D. "In the process, we'll also be developing vaccines that will protect people who would naturally acquire the viruses, as well as novel treatments for those who are already sick."

SFBR's BSL-4 maximum containment laboratory makes the Foundation a strong asset in researching deadly pathogens. The laboratory plays an important role in the national network of Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research, a program funded by the National Institute of Allergy and Infectious Diseases.

Funding sources for SFBR's programs include the National Institutes of Health (NIH) and the Defense Threat Reduction Agency of the U.S. Department of Defense, which recognize the need to be prepared to deal with the continuing threat of bioterrorism. NIH funding for biodefense research at SFBR in 2008 totaled $1.2 million, while Defense Department funding was more than $2.5 million.

## Ebola vaccine

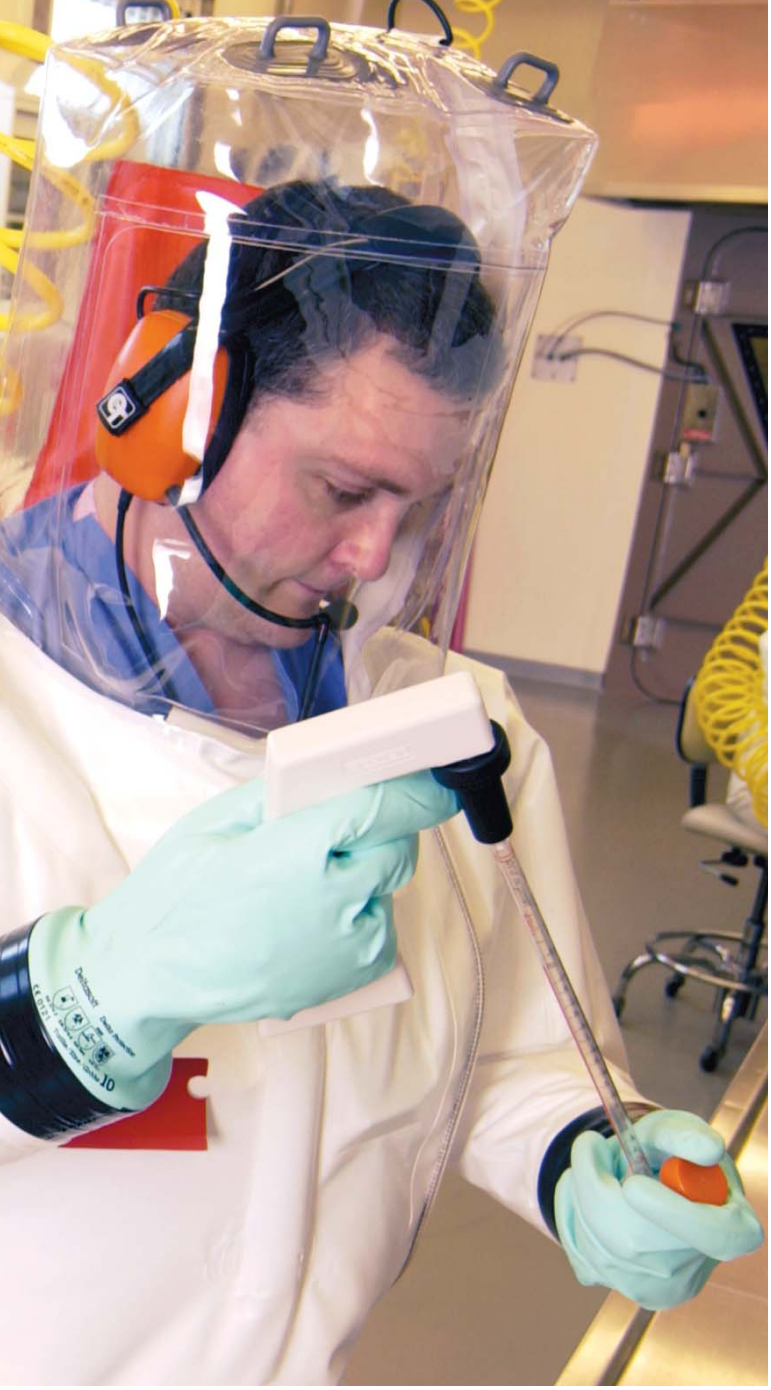
Development of a potential new vaccine to protect against the deadly Ebola virus is the most significant biodefense development over the past year at the Foundation, said Jean L. Patterson, Ph.D., chair of SFBR's Department of Virology and Immunology.

**Two high-dose VLP immunizations produced a high-level immune response in mice. When the twice-immunized mice were given a lethal dose of Ebola virus, they were completely protected from the disease.**

In its biodefense efforts, Patterson's department works with what the government calls "select agents," dangerous pathogens that are classified from "category A" to "category C." Those in category A are the most virulent and likely to be developed as bioterrorism weapons, and those in category C are the least likely. Ebola, for example, which can cause deadly hemorrhaging, is an example of a category A select agent.

A research team in which SFBR scientists played a prominent role reported findings in the January 2009 issue of the journal *Virology* indicating that protection against Ebola can be achieved by a vaccine produced in insect cells. In the new study, a vaccine using Ebola virus-like particles (VLPs) was produced in insect cells using traditional bioengineering techniques and injected into laboratory mice. A VLP vaccine is based on proteins produced in the laboratory that assemble into a particle that, to the human immune system, looks like the virus but cannot cause disease.

"The findings are significant in that the vaccine is not only extremely safe and effective but is also produced by a method already established in the pharmaceutical industry," said Carrion, one of the primary authors of the study in



*Andrew Hayhurst, Ph.D., in the BSL-4 lab.*

which Patterson also participated. "The ability to produce the vaccine efficiently is attractive in that production can be scaled up quickly in the case of an emergency, and doses can be produced economically."

Two high-dose VLP immunizations produced a high-level immune response in mice. When the twice-immunized mice were given a lethal dose of Ebola virus, they were completely protected from the disease. In contrast, mice that were not immunized had a very low immune-system response and became infected.

In another experiment, a three low-dose VLP immunization effectively boosted immune system response in mice and protected them against the Ebola virus. This finding is important because it demonstrates that since a small dose of vaccine produces immunity, many more vaccine doses can be generated compared with a poorly immunogenic vaccine.

VLPs are attractive candidates for vaccine development because they lack viral genomic material and thus are not infectious, are safe for broad application, and can be administered repeatedly to vaccinated individuals to boost immune responses.

The findings will be validated in additional animal systems. The vaccine will then undergo U.S. Food and Drug Administration (FDA) safety and efficacy testing before use in humans, which could occur in as few as five years.

Collaborators on the study included Richard Compans, Ph.D., and Chinglai Yang, Ph.D., of the Emory University School of Medicine in Atlanta.

Ebola viruses are considered a dangerous threat to public health because of their high fatality rate, ability to transmit person to person, and low lethal infectious dose. Moreover, their potential to be developed into biological weapons causes grave concern for their use as a bioterrorism agent. While some vaccines show protection in nonhuman primate studies, the strategies used may not be uniformly effective in the general human population due to pre-existing immunity to the virus-based vaccines.

Ebola viruses, which cause severe bleeding and a high fatality rate in up to 90 percent of patients, have no effective treatment or vaccine. Since the virus's first identification in Africa in 1987, Ebola outbreaks have caused some 1,800 human infections and 1,300 deaths. Outbreaks have become increasingly frequent in recent years and are likely to be caused by contact with infected animals followed by spread among humans through close person-to-person contacts. Ebola viruses cause acute infection in humans, usually within four to 10 days. Symptoms include headache, chill, and muscle pain, followed by weight loss, delirium, shock, massive bleeding, and organ failure, leading to death in two to three weeks.

## Development of the marmoset as a research model

Another significant advance at SFBR in research related to the Ebola studies and with applications for biodefense has been development of the marmoset as an animal model for hemorrhagic fevers. Animals such as the marmoset – a small, South American primate that typically weighs less

than a pound – fit better in laboratory settings than larger animals, and testing requires smaller doses of experimental antiviral compounds, which usually are in short supply.

"The smaller the animal, the smaller the amount of any compound you have to generate," Patterson said. "So if you're looking at lots of different new drugs, you want to use the smallest amount when you create that drug for a therapy. The same is true for vaccines. You don't want to have to create bulk amounts of something until you know it works."

Historically, marmosets have been considered difficult to breed and maintain in captivity.

However, Suzette Tardif, Ph.D., at the Southwest National Primate Research Center at SFBR, has developed husbandry, housing, and breeding standards, including standards for housing in high biocontainment, that have made the marmoset a premier nonhuman primate biomedical model. This animal is now readily maintained in captivity and useful for a variety of studies related to human health and disease.

An added benefit to working with marmosets is that they usually produce twins or triplets twice a year, making it easier to establish and maintain a colony.

Carrion's research team made further progress in 2008 in developing the marmoset as a model for biodefense research with a study involving Ebola and Marburg viruses. The viruses cause hemorrhagic fever and belong to a category of pathogen known as filoviruses. Infection with the viruses resulted in a disease syndrome very similar to that seen in infected humans.

Because the marmoset, although small, presents an immune response and symptoms similar to that found in people, word spread among scientists worldwide that it is a valuable new enhancement to research that could save millions of human lives. "We have already received inquiries from outside the country, so it's something that seems to be needed," Carrion said.

## Repurposing already approved drugs

SFBR scientists also continued in a nationwide discovery program in which the federal government is trying to find out if drugs already on pharmacy shelves, but approved for other purposes, could be used to treat infection with deadly pathogens. The program is funded by the Defense Department's Defense Threat Reduction Agency.

Carrion, the principal investigator on the subcontract to SFBR, said that with nearly 8,000 drug compounds known to clinical medicine, the likelihood is high that some could be effective against biothreat agents. He said the government especially would like to find a drug effective against multiple agents. That is important, he said, because in the event of an attack, doctors wouldn't immediately know what agent had been released, and many agents present the same initial symptoms.

The drugs, already approved by the FDA, are used for a variety of purposes. The idea is to go after drugs approved for safety to find out if they have antiviral or antibacterial activity.

## Lassa fever

Other ongoing biodefense research at SFBR includes work on two vaccines for Lassa fever, a virus that is thought to affect about a half a million persons per year in West Africa. It has up to a 15 percent mortality rate for those individuals who develop symptoms and can cause various complications in those who survive.

However, scientists do not know how many people are infected or how many people die from it because civil strife in the region prevents investigators from obtaining accurate data.

Lassa is spread by rodents, a common characteristic of its disease category, arenavirus.

"The rodents are the reservoir, meaning that they themselves do not get sick," Patterson said. "They have evolved with the virus, just as humans have evolved with viruses that don't make us sick. We only look for viruses that make us sick. And if you jump species, you often have an increase in pathogenesis to the species that has not co-evolved with that organism."

That is what makes Lassa virus a potentially dangerous bioterror weapon.

And that's what makes SFBR's research in biodefense so important. Its unique resources give SFBR scientists a safe environment in which to handle dangerous pathogens and be world leaders in the fight against emerging diseases and bioterror agents. This has allowed SFBR to expand its research programs and increase collaborations with other institutions worldwide in the effort to understand and cure baffling and deadly infectious diseases that observe no boundaries. ■

# SFBR Scientist Develops Baboon Model for Bone Diseases

SFBR's development of the baboon as a model for osteoporosis and osteoarthritis adds a powerful new weapon in the arsenal of scientists searching for ways to alleviate the suffering of millions of people. Osteoporosis and osteoarthritis are major causes of disability in the United States and are increasing in public health importance as its population ages. The world's largest pedigreed baboon colony is maintained by SFBR's Southwest National Primate Research Center and provides an unparalleled resource for research on these bone disorders.

Assistant Scientist Lorena M. Havill, Ph.D., of SFBR's Department of Genetics, was the lead author of a 2008 paper in the *Journal of Medical Primatology* titled "Osteopenia and osteoporosis in adult baboons." Michael Mahaney, Ph.D., a scientist in the Department of Genetics and the Southwest National Primate Research Center, also was part of the research team.

The paper demonstrated the value of the baboon as a model for osteoporosis, the fragile bone condition associated with aging, and osteopenia, the condition of low bone-mineral density that precedes osteoporosis. It is estimated that 10 million people in the United States have osteoporosis, and nearly 34 million are at increased risk for developing the disease.

"Baboons experience the same type of bone-related diseases that people do as they age," Havill said. The baboon model plays an important role in the collaboration between Havill and Dan Nicolella, an institute engineer in the Southwest Research Institute's Materials and Mechanical Engineering Division. "For our projects to work, it really takes equal leadership from both of us because we're merging his biomechanical and engineering expertise with my genetics and skeletal biology expertise," said Havill.

Nicolella, who has studied musculoskeletal biomechanics for more than 20 years, said, "I study why things break, what characteristics make them strong, how to design strong things. A lot of the same technology and techniques that we use in man-made, engineered structures we're applying to the musculoskeletal system."

**Baboons are a good model for osteoarthritis because they naturally develop the disease. It's a very common disease to see in baboons.**

*– Lorena M. Havill, Ph.D.*

Havill and Nicolella are in the process of developing a bone structural integrity profile with the goal of providing a new tool for assessing an individual's risk of bone fracture. They ultimately hope to be able to identify individuals who could benefit from early medical intervention to reduce their risk of fracture. In another project, the two scientists combine their strengths to study osteoarthritis, a painful degradation of the cartilage of the joints.

## Defining bone strength

For assessing bone fracture risk, the only current clinical option is the DXA scan, short for dual-energy X-ray absorptiometry, which determines the amount of mineral in a particular area. "But this only explains about 60 percent of bone strength," Havill said. "There are a lot of people with high bone mineral density who fracture and a lot of people with low bone mineral density who do not."

Nicolella is using computer modeling and engineering principles to come up with a diagnostic method that can be implemented in the clinic that includes not only the density of the bones from these scans, but also different aspects of the bone shape and structure that also affect bone fracture risk and bone strength.

*Lorena M. Havill, Ph.D.*

Assessing bone strength only from the mineral content is of little help from an engineering standpoint, Nicolella said. "That's like saying that we have 10 tons of steel in a bridge, so it's going to be strong. We want to know how the materials are distributed within that structure."

Funding for the bone structural integrity profile comes from a variety of sources including the Southwest Foundation Forum, the San Antonio Area Foundation, and the National Institutes of Health.

There is a strong genetics component to the studies. The ability to identify patients who may be genetically predisposed to fragile bones could allow doctors to intervene early by prescribing bone strengthening therapies and special exercises. Knowing the genes involved in risk also will aid scientists in the search for new pharmacologic therapies.

## Osteoarthritis

Even though it is estimated that 27 million people in the United States suffer from osteoarthritis, little is known about the cause of this painful condition. There is no treatment for this condition other than pain management.

"Baboons are a good model for osteoarthritis because they naturally develop the disease. It's a very common disease to see in baboons," Havill said, "just as occurs with people. Their behavior changes with the onset of osteoarthritis," she noted. "They move around less during cold or damp weather and climb less than they normally would." Havill has confirmed the condition in x-rays and then directly observed it in the bones of deceased baboons.

Havill and Nicollela are collaborating in research focused on osteoarthritis of the knee. This condition is more prevalent in women than men, especially as they approach menopause and afterwards. The pedigree data on the baboon bones provides rich material for studying the degree to which variation in knee osteoarthritis is genetic in a large pilot study of 300 animals.

Havill and Nicolella received funding for the pilot study from the Isis Fund for Sex-based Biology Research of the Society for Women's Health Research after completing a survey on knee osteoarthritis from veterinary records in 2008. They then hosted members of the Isis Fund Network for a discussion of these results and their implications for developing the baboon as a model for sex differences in osteoarthritis research.

As with osteoporosis, it would be of great benefit to identify individuals at elevated risk for osteoarthritis early in life. "By the time somebody comes into the clinic with it, they are far into the disease," Havill said. "There is so much that has gone wrong that you cannot identify the cause, and the ability to alleviate suffering is limited."

Havill and Nicolella hope that their combination of expertise in mechanical engineering and genetics applied to the baboon will lead to the clues that unlock the secrets of bone and joint disorders and lead to real answers for understanding, preventing, and treating these conditions. ■

# Cancer Model Aims at New Treatments

When John L. VandeBerg, Ph.D., arrived at the Southwest Foundation for Biomedical Research in 1980 to start a department of genetics, he brought 27 tiny marsupials and a big bundle of hope.

Now the Foundation's chief scientific officer, VandeBerg then had just begun a breeding program with the animals, mouse-sized South American opossums called *Monodelphis domestica*. As marsupials, adult opossums give birth to offspring that are still in an embryonic state, and VandeBerg had a hypothesis that the infant opossums could prove useful to study the early development of human diseases, especially cancer.

That bit of intuition has begun to pay dividends, particularly recently, when experiments by a young scientist in VandeBerg's laboratory showed that human cancer cells will grow and spread in immature newborn opossums until the developing animal's own immune system is activated. The study was published in February 2009 in the *International Journal of Clinical and Experimental Pathology* and opened the door to a potentially powerful new model for studying how human cancers spread and how the immune system mobilizes to fight them.

**The study . . . opened the door to a potentially powerful new model for studying how human cancers spread and how the immune system mobilizes to fight them.**

The research also demonstrates the importance of philanthropic support for those early studies to test the viability of new ideas. For the last 20 years, the San Antonio-based Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation has supported the SFBR opossum breeding colony, which now supplies laboratory animals to researchers around the globe. The Kleberg Foundation also has supported numerous biomedical studies using the opossums, including a grant that funded the research behind the discovery published in 2009.

"The Kleberg Foundation understands the need for a central animal resource that can serve the country and the world," said VandeBerg. "They also understand the importance of supporting biomedical research."

Researchers have long needed a model to study how human cancers spread throughout the body. Commonly used laboratory animals like mice have immune systems that recognize human cells as foreign objects, thereby preventing human cancers from growing in them. It is possible to grow human cancers in genetically altered mice with no immune systems, but the cancers do not spread in those mice as they do in people.

Staff scientist Zhiqiang Wang, M.D., Ph.D., who led the research at SFBR and is now at Methodist Hospital in Houston, decided to test what would happen in baby opossums, which are born without mature immune systems. He injected cells from human melanoma, prostate, and colon cancers into newborns and followed the development of the tumors. The cancers grew and spread very much as they do in humans, until the maturing animals' immune systems activated. The opossums' immune systems recognized the invading foreign cells and mobilized, causing the tumors to regress.

Other collaborators with Wang and VandeBerg included Gene Hubbard, D.V.M., a pathologist at SFBR.

VandeBerg hopes that the opossum will help doctors study how cancer manages to evade the immune system and spread throughout the body in humans.

"You basically have a war between the cancer cells trying to proliferate and the immune cells trying to stop the proliferation, and that is the process we want to understand," VandeBerg said. "We want to develop ways of strengthening the immune system so that it can defeat the cancer cells whereas in cancer patients now, it is struggling to do so and not succeeding."

The research also suggests a potential future diagnostic tool in which the animal could be used to find the optimal way of treating cancer in an individual patient. Such a tool could be used to assess the possible effect of a wide array of treatments such as chemotherapy, immune therapy, and gene therapy, VandeBerg said.

VandeBerg's involvement with the opossum dates back to his doctoral work in Australia, where he worked with a number of species of kangaroos. He returned to the United States in 1975 as a post-doctoral fellow at the University of Wisconsin, where he recognized the value of developing a small marsupial that could be raised in a laboratory and used to study developmental biology. In 1979, he got the chance to acquire 20 *Monodelphis domestica*, a native of Brazilian rainforests, and then got a $5,000 American Cancer Society grant through the university, proposing that the animals could be useful for studying cancer.

*Zhiqiang Wang, M.D., Ph.D., and John L. VandeBerg, Ph.D., with their opossum cancer model.*

He admits that he was stretching his imagination then in pursuit of financial support. "It is fitting that the American Cancer Society gave me the money to get the program started," VandeBerg said. "Eventually, it did become a very important animal for cancer research."

The big financial boost came the following year, when VandeBerg moved to San Antonio to establish a genetics department at SFBR. The Kleberg Foundation provided $200,000 to start the department, and those funds enabled VandeBerg to maintain the opossum colony and to conduct the first studies testing the scientific value of this new animal model.

In 1990, the Kleberg Foundation awarded a major $1 million grant to SFBR to start research into the genetics of susceptibility to cancer. The first major discoveries showed that the opossum is the only laboratory mammal that develops melanoma after exposure to ultraviolet light. Scientists are using the animal to understand how cells convert to black moles and then into melanoma. The Kleberg Foundation supports the colony with an annual grant of $400,000.

Scientists continue to find ways to use the laboratory opossum. SFBR is currently funded by a five-year $1.7 million grant from the National Institutes of Health to use the animals in a study of genetic control of blood cholesterol levels in response to cholesterol in the diet. Kleberg money also is supporting a pilot study to examine the animal as a model for research on the healing of spinal cord injuries, offering hope to the 11,000 people in the United States each year who suffer such devastating injuries. Those pilot studies show that the animals can regenerate nerve cells and recover normal function if the injury happens when the newborn opossums are a few days old. But if the injury happens after they are 12 days old, they do not recover. "We want to understand what genes are being turned on and off during that period. If we can learn how to manipulate those genes, we may be able to learn how to help people who have been paralyzed because of spinal cord injuries," VandeBerg said

Looking back to his fledgling colony of 1979, VandeBerg admitted that he never fully envisioned then just how important the tiny marsupial would become to scientists who are striving to understand complex human diseases.

"This shows the importance of helping scientists acquire the resources they need for those first early studies that test new ideas," VandeBerg said. "The American Cancer Society and the Kleberg Foundation have been vital partners in our research with this animal, and they deserve our deepest thanks." ■

# Don Taylor Oversees Special Research Animals

As a young man, Don Taylor, A.A., LATG, bounced through several jobs in search of his perfect career. He first trained as a mortician, later worked as a long-distance telephone operator, then moved to the San Antonio Zoo to work as a caretaker for penguins and flamingoes. He found his calling at last when his love of science brought him to the Southwest Foundation for Biomedical Research in 1980 as a laboratory assistant.

Now, some 29 years later, Taylor is an animal care supervisor in the Southwest National Primate Research Center. He oversees the daily care and detailed record-keeping for 2,500 laboratory rodents and marsupials that are vital to scientists studying the genetic underpinnings of cancer and other diseases. Supervisors and colleagues consider him an invaluable partner in ongoing and important research.

He would not have it any other way. "I'm very happy doing what I do," said Taylor, 51, who now directs a staff of four people. "I enjoy taking care of the animals, knowing they are in good health and good shape."

Taylor has won praise from both coworkers and professional peers in the field of animal care and management. Most recently, he was recognized in May 2009 by the Texas Branch of the American Association for Laboratory Animal Science for a presentation he made at the group's annual meeting. The presentation dealt with his specialty – the nurturing and maintenance of the species of South American opossums called *Monodelphis domestica* that are bred at the Foundation to supply researchers around the world.

Taylor has become a recognized expert in the care and breeding of these hamster-sized marsupials, which are native to Brazil. "Don has really been instrumental in the development of the *Monodelphis domestica* as a laboratory model," said John L. VandeBerg, Ph.D., the chief scientific officer of the Foundation. "He has been involved with them since way back in the beginning when we weren't quite sure how to care for them."

*SFBR's Don Taylor with a research guinea pig.*

In 1979, VandeBerg became one of the first researchers to attempt adapting the tiny opossums to the science laboratory. Taylor joined the *Monodelphis* research program in 1984 when scientists and animal care staff still were working to optimize the diet and environment to promote breeding and good health in captivity.

Work from those early days led to development of a commercial food that now is produced specifically for the South American opossum. Taylor and fellow caretakers

also figured out proper temperature and humidity and how to control environmental stress to keep opossum mothers content.

"He is dealing with a strange and unusual animal," said Larry B. Cummins, D.V.M., the Foundation's attending veterinarian and associate director of Southwest National Primate Research Center. "He has learned to treat them with a steady hand, to keep them from getting excited. In the wild, they are solitary animals. They are very sensitive and not very social, which was another issue to deal with in breeding them in captivity."

**A desire to provide the best possible care to research animals, which deserve good nutrition and clean housing, is Taylor's primary motivation.**

Laboratories from around the world now turn to Taylor's expertise when acquiring the opossums for their own scientists. "Don's excellent work led to development of a system, and now his system is used anywhere we send these animals," said Cummins.

It is a far cry from the employment prospects of his youth. Like many high school graduates, he was not sure what he wanted to do. Taylor got an associate's degree in mortuary science from San Antonio College and spent several years as a licensed mortician. The work was interesting but not fulfilling. He took a job as a phone operator, but kept looking for other opportunities.

"I always was interested in the natural sciences," he said. "Eventually, I took a job at the San Antonio Zoo, but I had already applied at the Foundation. About three months later, in September 1980, I was hired as a laboratory assistant with what was then the Department of Cellular and Molecular Biology."

The animals were fascinating, and the work in support of research was important. Taylor knew that he had found his career calling.

He spent the next several years working with different departments and different species, including baboons and chimpanzees. "That was a vastly different experience," he said of his work with the chimpanzees. "They are like rowdy teenagers. People don't realize that males can grow to be 180 pounds and be 10 times stronger than a human."

Taylor began working with the *Monodelphis* colony in 1984, and his responsibilities have grown significantly over the years. Now he and his four employees are charged with meticulous record-keeping that accompanies each animal from the day it is born. Many records are kept electronically, but a paper notebook still is fastened to each cage, where workers note meals, medications, observations, and study notes for each animal. He must make sure that records are in compliance with the federal agencies that oversee use of animals in research and that the Foundation follows all the guidelines on animal care set by the U.S. Department of Agriculture and other oversight groups.

It is a big paperwork trail that Taylor approaches methodically and professionally. "He is a quiet, very pleasant and hard-working guy," said Cummins. "Anything you go to check on in his area, he is doing it right."

Taylor also gets high marks as a supervisor who leads by doing his share of the work. "He is a working supervisor," VandeBerg said. "He takes the most challenging tasks for himself." He also assists scientists with some veterinary procedures on the research animals.

A desire to provide the best possible care to research animals, which deserve good nutrition and clean housing, is Taylor's primary motivation. "I don't think there is anyone involved in research who believes otherwise," he said. "The animals' welfare is of utmost importance, regardless of whether they are involved in a study. Researchers need healthy animals to get accurate results."

Away from the job, Taylor's focus is his family and home in San Antonio. He is an avid angler who builds vacations with his wife, Jonell, around fishing trips to the area lakes and the Gulf Coast. He also is a big fan of his 15-year-old daughter Sarah's volleyball team. "She is pretty good at it," he said.

Taylor never imagined his youthful interests in biology and wildlife would materialize into a fulfilling career. He enjoys working with animals and leading a team of animal caregivers who play a vital role in important research work at the Foundation.

"I have an enthusiastic group of young people that exhibit a genuine interest in the work we do here," Taylor said. "And I really enjoy coordinating the efforts of our investigators, veterinarians, technical, and animal care staff. I take pride in the fact that all of the animal care staff, supervisors, and veterinary staff here at the Foundation work extremely hard in caring for all of our animals." ■

# Translating Discovery

What would the world be like if Southwest Foundation scientists had not developed the high frequency ventilator which has saved the lives of thousands of premature babies? Or participated in the development of the hepatitis B vaccine, which is used in 116 countries to prevent a very disabling illness? Or served a major role in the development of oral contraceptives?

Scientific discoveries are literally made every day at the Foundation. While all of them are important, some eventually get translated into products that advance health care in our country and around the world. The process for translating discovery is called "technology transfer."

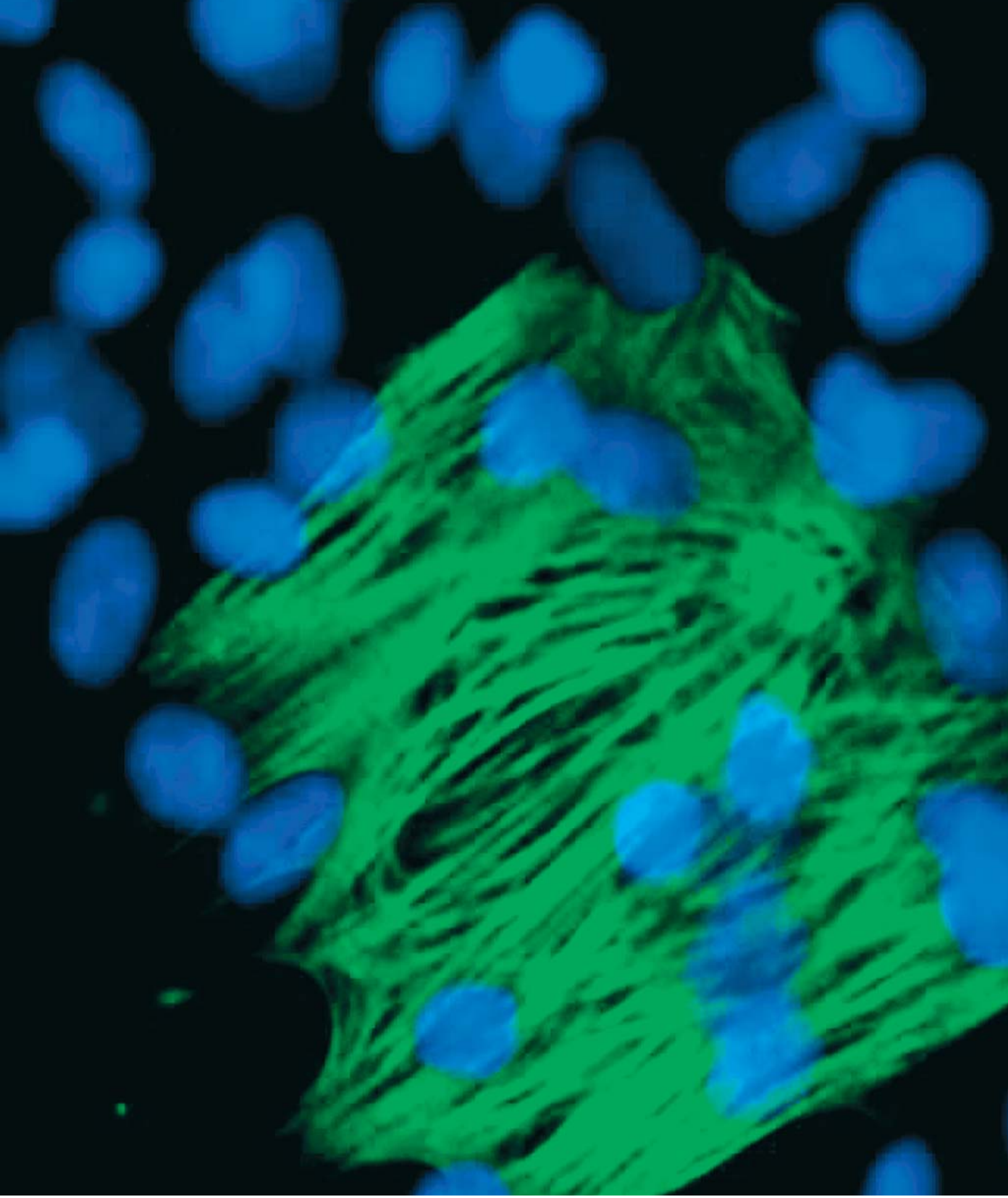
Technology transfer is the exchange of intellectual property (e.g., patents, know-how, trade secrets, and copyrights) through licensing, public disclosure of some kind, or other means from one person or entity to another in order to commercialize the underlying technology. Efforts to commercialize discoveries are implied in the Foundation's mission statement, which emphasizes "improving the health of our global community through innovative biomedical research."

On the horizon are several promising developments, from a diagnostic tool to predict a dangerous disorder in pregnant women – pre-eclampsia – to new approaches to prevent tuberculosis, the bacterial disease that affects one-third of the world's population. There is also real hope for an improved therapy to combat hepatitis C, the primary cause of liver cancer in this country. Women's health issues, such as safer birth control techniques and new treatments for breast cancer and post-menopausal disorders, are being pursued through the Foundation's spin-off company, Evestra™. Further down the road are possibilities for developing new treatments for schizophrenia, osteoarthritis, diabetes, heart disease, AIDS, malaria, Chagas disease, dengue fever, and a host of other conditions that threaten our own health and that of our neighbors throughout the world.

**Technology transfer does not just happen. It requires an infrastructure of skilled individuals who can identify promising technologies for commercialization, and protect those technologies through patent, copyright, or other means…**

Technology transfer does not just happen. It requires an infrastructure of skilled individuals who can identify promising technologies for commercialization; protect those technologies through patent, copyright, or other means; market the intellectual property to pharmaceutical or biotechnology companies; and negotiate appropriate licensing arrangements that are fair to the Foundation and to the public it serves. Key elements of an effective technology transfer process are a keen knowledge of where the science is headed, the best avenues for commercialization, how to value technologies that are often at an early stage, and the internal and external policy implications of a particular transaction.

The Southwest Foundation is investing additional dollars in technology transfer to improve human health and also to protect the value of its intellectual property assets. Over time, this investment can lead to additional revenue streams from royalties while assuring that significant disease conditions are addressed and ameliorated. ■



*Cultured smooth muscle cells derived from a baboon artery.*

# *The Year in Review*

Through a combination of outstanding research by its faculty, and a unique collection of scientific resources, including one of eight national primate research centers, the Southwest Foundation for Biomedical Research continues to have a profound impact on the health of our local and international communities. And given the greater understanding of how inherited traits influence our health and well-being, as well as the increasing danger of infectious diseases worldwide, the work of SFBR has become increasingly important in recent years.

With the leadership of Board Chair John R. Hurd, and the academic vision of John L. VandeBerg, Ph.D., the chief scientific officer and director of the Southwest National Primate Research Center, and Department Chairs Jean L. Patterson, Ph.D., and Sarah Williams-Blangero, Ph.D., the Foundation has maintained an intellectual vitality that marks it as one of the truly important independent, not-for-profit biomedical research organizations in the United States. Even in the face of restrained spending at the National Institutes of Health (NIH), SFBR has continued to effectively garner support for research projects in heart and circulatory disease, diabetes and obesity, AIDS, tuberculosis, hepatitis C, mental illness, and many other conditions that threaten the lives and the livelihood of people around the globe.

SFBR took several important steps in 2008 to guide its growth into the future. Highlights included securing a record research grant from NIH, the spin-off of the new pharmaceutical company Evestra™ and its first round of fund raising, a successful search for a new Foundation president, and important outreach to the San Antonio and scientific communities.

## Record grant awarded

SFBR received an $18.8 million federal research grant – the largest in the organization's history – to allow SFBR scientists to embark on several groundbreaking new studies

*Interim SFBR President John C. Kerr and Board Chair John R. Hurd.*

on cardiovascular disease that are unique in the world. The studies will use the unique pedigreed baboon resource at the Foundation and build upon the decades-long history of cardiovascular disease research with this model at SFBR.

"Some of the new projects we're undertaking are so innovative and rely so heavily upon the extraordinary resources and expertise of our facility that they're not simply on the cutting edge, they're actually cutting a new edge in scientific research," said VandeBerg, the grant's principal investigator. "We expect the payoff to be a tremendous advancement in our ability to prevent and treat cardiovascular disease, our nation's No. 1 killer."

## Evestra™ begins

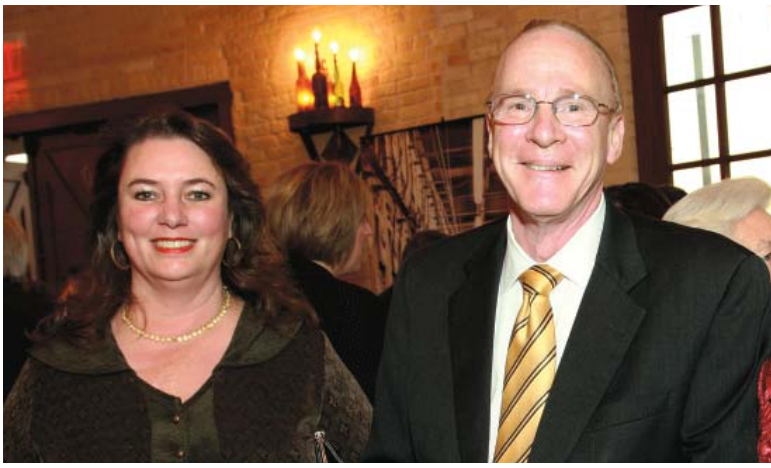
In early 2008 SFBR established Evestra™, transferring its Department of Organic Chemistry to this new for-profit company, which will focus on the development of new products for contraception, safer hormone replacement therapy, the treatment of endometriosis and fibroid tumors, the treatment of hormonally dependent breast cancer, and other women's health issues. The announcement was described in a *San Antonio Express-News* editorial as "good news for San Antonio's biomedical industry. The spinoff will boost the city's stature in the biomedical field and has tremendous potential to help the foundation financially."

For SFBR, the majority stockholder in the new company, it means there are potential financial gains as the value of its holdings increases. That will benefit the Foundation's endowment, which provides a source of support for all of SFBR's basic, not-for-profit biomedical research. And the members of the former Department of Organic Chemistry now have a tremendous opportunity to take the large body of work they have accumulated, along with their sense of innovation, and apply it toward the development of marketable health care products under the guidance of an expert management team operating in both San Antonio and Germany.

## New SFBR president named

Following a year-long search process, the SFBR board hired Kenneth P. Trevett in July as its new president and chief executive officer. In late September, he succeeded former Board Chair John C. Kerr, who had served as interim president since June of 2006.

Trevett, an attorney, comes to the position with 26 years of senior management experience at independent research



*Sarah Williams-Blangero, Ph.D., and Kenneth P. Trevett.*

institutes such as SFBR, including his most recent position as president of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center (LA BioMed), one of the largest independent biomedical research organizations in California. Previously, he served as a senior administrator and legal counsel for The Schepens Eye Research Institute in Boston and as general counsel of the Dana-Farber Cancer Institute in Boston – both affiliated with Harvard Medical School – and assistant to the director and house counsel of The Jackson Laboratory in Bar Harbor, Maine.

In addition to his responsibilities at LA BioMed, Trevett has served on numerous city and state research and economic development boards, and in the 1990s, he was elected to a two-year term as president of the Association of Independent Research Institutes (AIRI), the national coalition of SFBR's peer organizations.

Trevett's plans at SFBR include enhancing its collaborative research environment, developing a sophisticated technology transfer program for the commercialization of promising technology in the patient care arena, leading the organization through a building program to create more space and opportunities for its scientists, and raising its profile locally and nationally.

## Outreach to San Antonio and beyond

Kerr and Trevett built strong relationships during 2008 with other research organizations, with an eye to strengthened collaborations, both now and in the future. Kerr served as chair of the Texas Biological and Agro-Defense Consortium and was a board member on the boards of the San Antonio Medical Foundation, the Texas

*Juvenile baboons at Southwest National Primate Research Center.*

Research and Technology Foundation (TRTF), and BioMed SA. Trevett served on the board of BioMed SA and of TRTF, the advisory board of the Southwest Research Institute, and as a member of the Advisory Committee of South Texas Accelerated Research Therapeutics. SFBR is an active member of AIRI and played a significant role at its 2008 annual meeting. SFBR also was a member of Research!America, a nonpartisan alliance in support of public education and advocacy to make health research a higher national priority; the Scientists' Center for Animal Welfare; and BioMed SA.

In other outreach activities, during January, February, and March, the Southwest Foundation Forum hosted on the SFBR campus 10 classes of high school seniors in advanced placement biology and chemistry. Their visits exposed students to the exciting possibilities of a science career by viewing a video overview of the Foundation, peeking into its laboratories, and interviewing SFBR scientists working on hepatitis C, heart disease, diabetes, obesity, lung disease in premature infants, and other health problems. Separate tours also were organized for members of the Greater San Antonio Chamber of Commerce's Leadership San Antonio and Health Care and Biosciences Committee, which was chaired by Corbett Christie, SFBR's vice president for institutional advancement.

## Lanford co-organizes hepatitis C meeting

SFBR scientist Robert E. Lanford, Ph.D., served as a co-organizer of the 15th International Symposium on Hepatitis C and Related Viruses that brought 800 scientists to San Antonio from October 5–9. At the symposium, 450 presentations by scientists from around the world provided an overview of the history of the hepatitis C virus (HCV) and current statistics on disease prevalence and trends, as well as the latest in biomedical research aimed at treating and preventing HCV infections. Worldwide, approximately 170 million people are believed to be infected with HCV, and approximately 3.2 million people in the United States are believed to be chronically infected. Hepatitis C infection is already the leading cause of liver transplants in this country, and now the United States is also experiencing an increase in the rate of HCV-related liver cancer.

The meeting was timely because HCV researchers worldwide are urgently trying to develop an antiviral treatment to replace the only U.S. Food and Drug Administration-approved therapy for HCV infection, a 48-week, two-drug regimen that causes severe flu-like symptoms and a number of other side effects. The cure rate is less than 50 percent for those who endure the side effects of the two drugs and complete treatment.

## Looking ahead

The forethought and strategic planning of past SFBR leaders has enabled it to undertake many of the exciting initiatives described in this brief look at the year 2008. With the guidance of the board of trustees, SFBR continues to build for the future by identifying key issues, opportunities, and challenges that the organization will face in the coming years. One of these is a building program to give SFBR scientists better space to continue to conduct their first rate science and to attract to its faculty the best minds in genetics, virology and nonhuman primate research. This will markedly enhance SFBR's ability to improve the health of people around the globe. ■

# New Grants and Contracts

| Grant Sponsor, Title, SFBR Principal Investigator, Length of Grant | Total Amount to SFBR |
|---|---|

## Federal Research Grants and Contracts

| | |
|---|---|
| *National Institutes of Health*<br>Diet and Genotype in Primate Atherosclerosis<br>Dr. John L. VandeBerg, 5 Years | $ 18,833,512 |
| *National Institutes of Health*<br>Genetics of Atherosclerosis in Mexican Americans<br>Dr. John Blangero, 5 Years | $ 12,473,941 |
| *National Institutes of Health*<br>Identification of Genes Influencing Total Antioxidant Status<br>Dr. John Blangero, 5 Years | $ 3,106,372 |
| *National Institutes of Health*<br>Genetic Determinants of Human Transcriptional Aging<br>Dr. Sarah Williams-Blangero, 5 Years | $ 2,786,299 |
| *National Institutes of Health*<br>Genetic Analysis of Common Disease: An Evaluation<br>Dr. Laura Almasy, 5 Years | $ 2,363,571 |
| *National Institutes of Health*<br>A Neurobehavioral Family Study of Schizophrenia<br>Dr. Laura Almasy, 5 Years | $ 1,812,067 |
| *National Institutes of Health*<br>Genetics of Gallbladder Disease in Mexican Americans<br>Dr. Ravindranath Duggirala, 4 Years | $ 1,610,839 |
| *National Institutes of Health/University of Texas Health Science Center Houston*<br>Genetics of Brain Structure and Function: Genome-Wide Association<br>Dr. John Blangero, 5 Years | $ 1,503,445 |
| *Navy Engineering Logistics Office*<br>Task 2079, Foodborne Threat Assessment RFP No. N47156-06-C-5555-P00005 06-1495 Supplement<br>Dr. Jean L. Patterson, 1 Year | $ 1,278,908 |
| *National Institutes of Health/Seattle Biomedical Research Institute*<br>Factors Influencing Oral Transmission of SIV<br>Dr. Luis D. Giavedoni, 4 Years | $ 1,071,728 |
| *National Institutes of Health/University of North Carolina*<br>Comprehensive Mapping of a Blood Pressure QTL on Chr 17<br>Dr. Sue Rutherford, 3 Years | $ 1,001,203 |
| *National Institutes of Health/University of Texas Health Science Center San Antonio*<br>Identification of Prediabetes Genes by Expression Linkage Analysis<br>Dr. Joanne E. Curran, 5 Years | $ 634,367 |
| *Department of Defense*<br>Discovery of New Therapeutic Leads for Prostate Cancer<br>Dr. Susan L. Mooberry, 3 Years | $ 627,076 |
| *National Institutes of Health/Magee Womens Research Institute & Foundation*<br>Rhesus Propagation by Intracytoplasmic Nuclear Injection & Pluripotent Stem Cells<br>Dr. Karen Rice, 5 Years | $ 592,152 |
| *National Institutes of Health/University of Connecticut Health Science Center*<br>Genetics of Cocaine Dependence<br>Dr. Laura Almasy, 5 Years | $ 562,907 |
| *Defense Threat Reduction Agency/Peregrine Pharmaceuticals, Inc.*<br>Anti-phosphatidylserine Antibodies as Therapeutics for Hemorrhagic Fever Virus Infections<br>Dr. Ricardo Carrion Jr., 1 Year | $ 491,170 |

| Grant Sponsor, Title, SFBR Principal Investigator, Length of Grant | Total Amount to SFBR |
|---|---|
| *National Institutes of Health*<br>Heat Stable Filoviral Diagnostics<br>Dr. Andrew Hayhurst, 2 Years | $ 470,250 |
| *National Institutes of Health/Pan Thera Biopharma*<br>Development of a Recombinant Subunit Ebola Vaccine<br>Dr. Jean L. Patterson, 2 Years | $ 407,501 |
| *Naval Research Laboratories*<br>Development and Testing of Recombinant Single Domain Antibodies Supplement<br>Dr. Andrew Hayhurst, 2 Years | $ 393,000 |
| *National Institutes of Health/Emory University*<br>Novel Vaccine Strategies Against Ebola Virus<br>Dr. Jean L. Patterson, 3 Years | $ 295,154 |
| *National Institutes of Health*<br>Southwest National Primate Research Center Supplement<br>Mr. John C. Kerr, 1 Year | $ 267,187 |
| *National Institutes of Health/University of New Mexico/University of Texas Medical Branch Galveston*<br>Western Regional Center of Excellence for Biodefense and Emerging Infectious Diseases: Small Animal Core Supplement<br>Dr. Jean L. Patterson, 1 Year | $ 200,370 |
| *National Institutes of Health*<br>Development of Hepatitis C Virus-like Particles as Candidate HCV Vaccine<br>Dr. Krishna K. Murthy, 1 Year | $ 166,768 |
| *National Institutes of Health/University of Texas Health Science Center San Antonio*<br>Effect of Chronic Inflammation on Atherosclerosis Outcomes in RA<br>Dr. Ravindranath Duggirala, 5 Years | $ 152,726 |
| *Department of Defense/Emory University*<br>Foodborne Anthrax Threat Assessment Supplement<br>Dr. Jean L. Patterson, 5 Months | $ 146,500 |
| *National Institutes of Health/Emory University*<br>SPF Breeding Colonies at the Yerkes National Primate Research Center<br>Dr. Jeff Rogers, 5 Years | $ 112,032 |
| *National Institutes of Health/University of Texas Medical Branch Galveston*<br>Development of Bupropion for Smoking Cessation During Pregnancy<br>Dr. Karen Rice, 3 Years | $ 93,528 |
| *National Institutes of Health*<br>Genetic Analysis of Idiopathic Thrombosis Supplement<br>Dr. Laura Almasy, 1 Year | $ 89,123 |
| *National Institutes of Health/University of Maryland*<br>Recombinant Yellow Fever 17D-Lassa Vaccine<br>Dr. Jean L. Patterson, 1 Year | $ 79,345 |
| *US Air Force/National Institutes of Health*<br>DNA Aptamer Testing Supplement<br>Dr. Ricardo Carrion Jr., 9 Months | $ 76,593 |
| *National Institutes of Health/University of Texas Health Science Center Houston*<br>Center for Disease Control and Prevention: Centers for Public Health Preparedness<br>Ms. Jean Frazier, 6 Months | $ 49,000 |
| *National Institutes of Health/University of Texas Health Science Center San Antonio*<br>The Disablement Process in Rheumatoid Arthritis<br>Dr. Ravindranath Duggirala, 5 Years | $ 36,358 |

| Grant Sponsor, Title, SFBR Principal Investigator, Length of Grant | Total Amount to SFBR |
|---|---|
| *National Institutes of Health/Stanford Research Institute*<br>Broad-Spectrum Agents for Prophylaxis and Treatment Against Bacterial Threats<br>Dr. Ricardo Carrion Jr., 2 Years | $ 25,000 |
| *U.S. Army/ITT Industries*<br>ECBC Survival Study Supplement<br>Dr. Ricardo Carrion Jr., 1 Year | $ 7,500 |
| *National Institutes of Health*<br>Development of Hepatitis C Virus-like Particles as Candidate HCV Vaccine<br>Dr. Krishna K. Murthy, 1 Year | $ 4,095 |
| **TOTAL FEDERAL RESEARCH GRANTS AND CONTRACTS** | **$ 53,821,587** |

## Miscellaneous Research Grants and Contracts

| | |
|---|---|
| *Stanford Research Institute*<br>An Accelerated Path to Safe and Effective Therapeutics APSET for Bioterrorism Agents Mouse Bacterial Testing<br>Dr. Ricardo Carrion Jr., 8 Months | $ 211,182 |
| *University of Texas Health Science Center San Antonio*<br>Assessments of the Beta Cell Function Achieved by Hemipancreatectomy Using Hyperglycemic Clamp Technique in a Nonhuman Primate Model<br>Dr. Raul A. Bastarrachea, 8 Months | $ 58,732 |
| *Barshop Institute for Longevity and Aging Studies*<br>Screening of MarMonthset Colony for GBV-A and Lymphotropic Callitrichid Virus LCV<br>Dr. Robert E. Lanford, 1 Year | $ 36,666 |
| *University of Texas Health Science Center San Antonio*<br>Measuring Autoacoustic Emissions in Marmosets: Age and Sex<br>Dr. Kathleen M. Brasky, 1 Year | $ 31,654 |
| *Children's Mercy Hospital*<br>Development of Primate Model for Evaluation of Tissue Engineered Heart Valve in Baboon<br>Dr. Kathleen M. Brasky, 2 Years | $ 28,979 |
| *Universidad Autonoma de Yucatan-Clinical de Merida*<br>Genetic Variation of SEPS1: Its Influence on Obesity-Related Inflammatory Cytokyne Production in Yucatecan Individuals<br>Dr. Raul A. Bastarrachea, 1 Year | $ 23,135 |
| *University of Texas Health Science Center San Antonio*<br>Statistical Data for the E-FIND Project<br>Dr. Anthony Comuzzie, 1 Year | $ 22,207 |
| *University of Texas Health Science Center San Antonio*<br>Personnel Funding – Dr. Susan Mooberry<br>Dr. Robert E. Shade, 4 Months | $ 21,474 |
| *International Center for Medical Research and Training*<br>Association Studies to Identify Candidate *Plasmodium falciparum* Drug Resistance Molecular Markers in the Colombia Pacific Coast<br>Dr. Timothy J. C. Anderson, 6 Months | $ 20,000 |
| *University of Texas Health Science Center San Antonio*<br>Development of an Off-Pump Coronary Artery Bypass in NHPs to Evaluate the Effect of Botox on the Flow of Arterial Grafts<br>Dr. Cheryl DiCarlo, 2 Years | $ 18,542 |
| *Wake Forest University*<br>Personnel Funding – Dr. Anthony Comuzzie<br>Dr. Anthony Comuzzie, 1 Year | $ 8,906 |

| Grant Sponsor, Title, SFBR Principal Investigator, Length of Grant | Total Amount to SFBR |
|---|---|
| *University of Texas Health Science Center San Antonio*<br>Statistical Genetic Analysis of Data Provided Using SOLAR<br>Dr. Ravindranath Duggirala, 6 Months | $ 7,675 |
| *University of Texas Health Science Center San Antonio*<br>Effects of Aging on Vaccine Efficacy in Baboons<br>Dr. Karen Rice, 7 Months | $ 6,275 |
| **TOTAL MISCELLANEOUS RESEARCH GRANTS AND CONTRACTS** | **$ 495,426** |

## Philanthropic Research Grants

| | |
|---|---|
| *Robert J. Kleberg Jr. & Helen C. Kleberg Foundation*<br>Chagas Disease: An Emerging Fatal Disease in Texas<br>Dr. John L. VandeBerg, 1 Year | $ 399,000 |
| *Robert J. Kleberg Jr. & Helen C. Kleberg Foundation*<br>*Monodelphis* Research Program<br>Dr. John L. VandeBerg, 1 Year | $ 398,943 |
| *American Heart Association*<br>Investigating a Chr 18 Region for Involvement in Hypertension and Systolic BP<br>Dr. Sue Rutherford, 4 Years | $ 308,000 |
| *Cystinosis Research Foundation*<br>Scanning the Human Transcriptome in Cystinotic Cell Lines for Changes That Are Associated with Genetic Variation in the CTNS Gene<br>Dr. Eric Moses, 2 Years | $ 183,470 |
| *George W. Brackenridge Foundation*<br>Postdoctoral Fellowship<br>Dr. Paul Higgins, 1 Year | $ 106,672 |
| *Max & Minnie Tomerlin Voelcker Fund*<br>Pedigreed Baboon Colony Support<br>Dr. John L. VandeBerg, 1 Year | $ 100,000 |
| *Coates Foundation*<br>Genetic Dissection of Cystinosis: An Innovative Program for Novel Mechanism/Gene Discovery<br>Dr. Eric Moses, 1 Year | $ 75,650 |
| *Morrison Trust*<br>Protein Biomarkers for Early Detection of Liver Cancer<br>Dr. Robert E. Lanford, 1 Year | $ 59,722 |
| *Cowles Memorial Trust*<br>Postdoctoral Fellowship<br>Dr. Matthew Johnson, 1 Year | $ 55,060 |
| *Cowles Memorial Trust*<br>Postdoctoral Fellowship<br>Dr. April Risinger, 1 Year | $ 52,538 |
| *Cowles Memorial Trust*<br>Postdoctoral Fellowship<br>Dr. Claire Bellis, 1 Year | $ 50,676 |
| *Max & Minnie Tomerlin Voelcker Fund*<br>The Effects of Diet and Obesity on Prostate Specific Antigen PSA in Nonhuman Primates<br>Dr. James Mubiru, 1 Year | $ 50,000 |

| Grant Sponsor, Title, SFBR Principal Investigator, Length of Grant | Total Amount to SFBR |
|---|---|
| *Joe and Jessie Crump Foundation*<br>Cancer Research<br>Dr. Robert E. Lanford, 1 Year | $ 50,000 |
| *Max & Minnie Tomerlin Voelcker Fund*<br>Genetics of Oxidative Stress Markers and Their Correlation with Cardiovascular and Metabolic Syndrome Related Phenotypes in Mexican American Children<br>Dr. Vidya S. Farook, 1 Year | $ 49,697 |
| *Max & Minnie Tomerlin Voelcker Fund*<br>Opossum Model of Nonalcoholic Fatty Liver Disease<br>Dr. Rampratap S. Kushwaha, 1 Year | $ 49,550 |
| *Max & Minnie Tomerlin Voelcker Fund*<br>Identification of Genetic Regulators Influencing Acute Myeloid Leukemia Development<br>Dr. Melanie Carless, 1 Year | $ 49,354 |
| *Max & Minnie Tomerlin Voelcker Fund*<br>Defining High Risk Heart Disease Genomic Profiles for Potential Interventions<br>Dr. Laura A. Cox, 1 Year | $ 49,330 |
| *Max & Minnie Tomerlin Voelcker Fund*<br>Creation of Immortalized Chimpanzee and Baboon Hepatocyte Cell Lines for Analysis of HCV Associated Disease and Liver Cancer<br>Dr. Robert E. Lanford, 1 Year | $ 47,758 |
| *Southwest Foundation Forum*<br>Systematic Identification of Herpes B Virus Encoded MicroRNAs Using Deep Sequencing Technology<br>Dr. Anthony Griffiths, 1 Year | $ 35,000 |
| *Southwest Foundation Forum*<br>Epidemiologic Investigation of Tuberculosis in a Mexican Population from Chihuahua State, Mexico: A Pilot Study<br>Dr. Ravindranath Duggirala, 1 Year | $ 35,000 |
| *Max & Minnie Tomerlin Voelcker Fund*<br>Investigation of Gene Expression in Systolic Blood Pressure<br>Dr. Sue Rutherford, 1 Year | $ 34,996 |
| *Semp Russ Foundation of the San Antonio Area Foundation*<br>Role of Chromosome 11 in Blood Pressure Variation<br>Dr. Sue Rutherford, 1 Year | $ 34,969 |
| *Southwest Foundation Forum*<br>Early Mechanism of HIV Transmission Using the SIV/Macaque Model for AIDS<br>Dr. Marie-Claire Gauduin, 1 Year | $ 34,900 |
| *Semp Russ Foundation of the San Antonio Area Foundation*<br>Genomic Methylation Status in Diabetes<br>Dr. Melanie Carless, 2 Years | $ 34,830 |
| *Southwest Foundation Forum*<br>Searching for Aminopeptidase Gene Variants and their Contribution to Pre-eclampsia Susceptibility<br>Dr. Matthew Johnson, 1 Year | $ 34,790 |
| *Max & Minnie Tomerlin Voelcker Fund*<br>DNA Damage Repair Capacity, Cancer Incidence, and Survival in the San Antonio Family Heart Study<br>Dr. Jack Kent Jr., 1 Year | $ 34,775 |

| Grant Sponsor, Title, SFBR Principal Investigator, Length of Grant | Total Amount to SFBR |
|---|---|
| *Southwest Foundation Forum* | |
| Gene Expression Across Tissues in Obese and Non-Obese Baboons<br>Dr. Elizabeth Tejero, 1 Year | $ 34,626 |
| *Max & Minnie Tomerlin Voelcker Fund* | |
| Sequence Capture for Comprehensive Re-Sequencing of a Chromosomal Region Encoding a CVD-Related QTL<br>Dr. Karin Haack, 1 Year | $ 32,690 |
| *Southwest Foundation Forum* | |
| Effects of Maternal Nutrient Restriction on Fetal Bone Development<br>Dr. Lorena M. Havill, 1 Year | $ 27,525 |
| *Semp Russ Foundation of the San Antonio Area Foundation* | |
| Association Between Genetic Variation in Diabetes-related Genes and Energy Metabolism in Hispanic Children<br>Dr. Elizabeth Tejero, 1 Year | $ 13,740 |
| **TOTAL PHILANTHROPIC RESEARCH GRANTS** | **$ 2,523,261** |
| **TOTAL COMMERCIAL, NON-FEDERAL RESEARCH GRANTS AND CONTRACTS** | **$ 3,635,640** |
| **TOTAL RESEARCH GRANTS AND CONTRACTS** | **$ 60,475,914** |

## Construction and Renovation Grants

| | |
|---|---|
| *National Institutes of Health* | |
| Renovation of Building 4 to Provide BSL-2 Housing for AIDS Research<br>Dr. John L. VandeBerg, 1 Year | $ 443,130 |
| **TOTAL CONSTRUCTION AND RENOVATION GRANTS** | **$ 443,130** |
| **TOTAL GRANTS AND CONTRACTS AWARDED TO SFBR IN 2008** | **$ 60,919,044** |

# *Sources of SFBR Funding*

Despite the economic crisis, the Southwest Foundation for Biomedical Research continued to enjoy a strong financial position in 2008. This was due to the hard work and ingenuity of SFBR's world-class scientists and the strong heritage of support from donors. These factors, combined with prudent investment choices and disciplined internal oversight and effective financial controls and systems, have contributed to SFBR's financial stability.

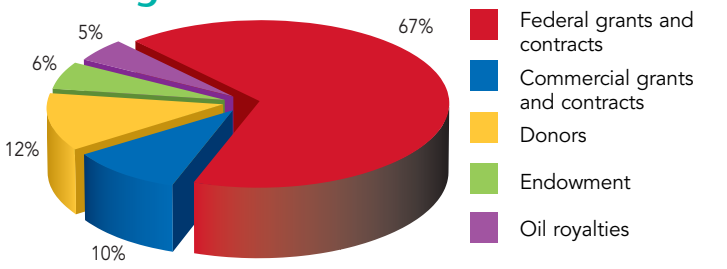
Ernst & Young audited SFBR's operations for the fiscal year ending December 31, 2008, and had no audit adjustments. The firm's audited financial statements for SFBR are included in this section on pages 38 and 39.

In 2008, 66 percent of SFBR's $51 million operating budget was funded through highly competitive, peer-reviewed research grants and contracts from the National Institutes of Health (NIH) and other federal agencies. Meanwhile, the organization's scientific expertise and extraordinary research resources were instrumental in securing commercial contracts with biotechnology firms and pharmaceutical companies equal to 10 percent of SFBR's budget.

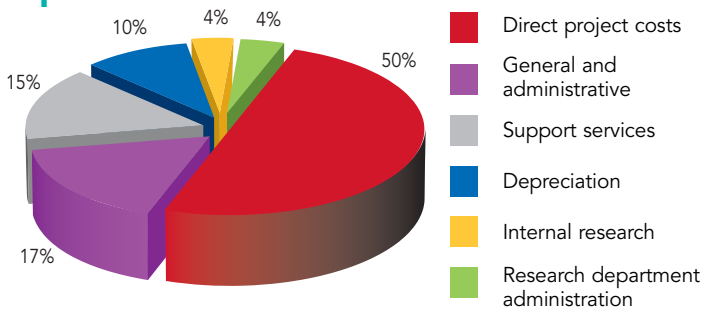
As the accompanying chart shows, philanthropy continues to play the vital role in SFBR research that Tom Slick envisioned when he founded the organization in 1941. Altogether, philanthropy constituted nearly 23 percent of the Foundation's revenues. Sources included 12 percent from yearly philanthropic contributions, 6 percent from SFBR's endowment, and 5 percent from oil and gas revenues. This makes SFBR and its donors true partners in scientific progress.

Financial support from donors enables SFBR to attract and retain the world's top scientists, provide researchers with state-of-the-art technology and laboratories needed to advance their work, and launch innovative pilot projects to explore new ways to understand and eliminate diseases. Private gifts also leverage significant additional investment by allowing investigators to compete successfully for prestigious foundation grants that do not cover the full cost of research. Important SFBR sources of philanthropic funding include the Golden Circle, the Southwest Foundation Forum, the Founder's Council, and annual contributions from Argyle members.

## Funding in 2008




## Expenses in 2008




In addition to these current contributions, SFBR research is supported through annual earnings on previous philanthropic gifts to the Foundation. At the end of fiscal year 2008, SFBR's endowment was valued at a total of $70.4 million, which is $21.4 million less than 2007, a result of the overall downturn in the market during this time. SFBR's investment strategy, which is designed to protect principal while providing for reasonable growth, is guided by the Investment Committee of the Board of Trustees. Although SFBR has had losses, the decline in the endowment was not as large as that experienced by many other not-for-profit research organizations and universities.

In 2008, SFBR also received significant royalties on oil and gas properties that had previously been contributed by donors. This revenue was critical to Foundation programs at a time when other sources were under stress.

While SFBR's reserves remain strong, flatlined NIH funding for scientists and delays in grant approvals from the agency present continuing challenges. Careful stewardship of existing funds and creative approaches to new sources of revenue will be important to the continuing success of the Foundation. ■

# *Audited Consolidated Balance Sheets (as of December 31, 2008)*

## ASSETS

| | December 31 2008 | 2007 |
|---|---|---|
| Cash and cash equivalents | $ 10,188,035 | $ 1,304,666 |
| Receivables: | | |
| Accounts | 357,352 | 221,994 |
| Contracts receivable from research projects | 8,850,918 | 8,219,349 |
| Amounts due on authorized grants in aid: | | |
| National Institutes of Health | 22,914,981 | 19,815,531 |
| Other | 10,108,548 | 8,430,353 |
| Prepaid expenses and supplies | 161,245 | 120,270 |
| Contributions receivable | 999,227 | 1,710,060 |
| Commercial paper – unrestricted | – | 5,000,000 |
| Assets limited as to use: | | |
| Cash | 3,751,329 | 152,423 |
| Investments | 70,362,244 | 91,802,821 |
| Commercial paper – restricted | – | 3,594,512 |
| Assets limited as to use – other | 48,715 | 85,899 |
| The Argyle land, buildings, and equipment (net of accumulated depreciation of $2,934,755 and $2,734,243 in 2008 and 2007, respectively) | 3,675,859 | 2,293,663 |
| Property, plant, and equipment: | | |
| Land | 374,530 | 374,530 |
| Buildings and improvements | 46,826,320 | 46,161,487 |
| Fixtures and equipment | 47,954,877 | 46,548,148 |
| | 95,155,727 | 93,084,165 |
| Less allowances for depreciation | 49,345,766 | 44,723,957 |
| | 45,809,961 | 48,360,208 |
| Construction in progress | – | 215,736 |
| | 45,809,961 | 48,575,944 |
| **Total assets** | **$ 177,228,414** | **$ 191,327,485** |

# *Audited Consolidated Balance Sheets* *(as of December 31, 2008)*

## LIABILITIES AND NET ASSETS

| | December 31 2008 | 2007 |
|---|---|---|
| Accounts payable and accrued expenses: | | |
| Trade accounts | $ 2,081,414 | $ 1,988,902 |
| Accrued wages, vacation, and other liabilities | 2,278,866 | 1,817,700 |
| Convertible promissory notes and accrued interest | 4,042,500 | – |
| Note payable | 675,000 | – |
| Postretirement benefits | 651,608 | 613,896 |
| Unearned contract revenue from research projects | 6,257,962 | 4,711,099 |
| Amounts unearned on grants in aid: | | |
| Advance collections | 250,942 | 346,565 |
| Uncollected authorized grants in aid | 27,053,625 | 24,426,186 |
| **Total liabilities** | **$ 43,291,917** | **$ 33,904,348** |
| | | |
| Net assets: | | |
| Unrestricted net assets | 91,264,288 | 117,950,698 |
| Temporarily restricted net assets | 15,904,979 | 8,933,673 |
| Permanently restricted net assets | 26,767,230 | 30,538,766 |
| **Total net assets** | **$ 133,936,497** | **$ 157,423,137** |
| | | |
| **Total liabilities and net assets** | **$ 177,228,414** | **$ 191,327,485** |

# *Why Support SFBR?*

It's a fact of life that grants and other income are insufficient for SFBR to achieve its important mission. Since the organization's founding, giving has played the role of a powerful enabler of progress, making philanthropy one of the cornerstones of the success of this institution. Here are a few examples of how your financial support can make all the difference to SFBR scientists:

- **Leverage**. On average, for every $1 contributed, SFBR scientists gain another $8 in competitive grant support, making Foundation researchers among the most productive anywhere.
- **Critical programs and projects**. Research grant and contract funding is the majority funding source of SFBR, totaling about 75 percent of revenue. The remaining support must come from endowment income and current donations.
- **Key research ventures**. Donations fund recruitment of key scientists and pilot studies, each representing strategies that encourage bold initiatives by new and existing faculty.
- **Extraordinary resources**. SFBR has a history of developing rare scientific resources. The AT&T Genomics Computing Center and the BSL-4 maximum containment laboratory are examples of such resources funded by donations.
- **Technology**. Modern research is made more productive by the latest technology. The higher cost of the newest technology usually requires philanthropic support.
- **Making the difference**. Unlike some research organizations, SFBR does not have patient or tuition revenue to fund capital and operating expenses. Donations are critical for funding new programs and capital purchases at SFBR.

SFBR excels as a center for scientific research because of the philanthropic support of donors. Will you consider becoming a partner in progress? In addition to donor opportunities highlighted in this report, such as the Golden Circle, The Argyle, Founder's Council, and Southwest Foundation Forum, the Foundation offers opportunities for legacy gifts, capital and endowment gifts, and memorial and honor gifts.

For more information on any of these giving opportunities, please contact SFBR's vice president for instititional advancement, Mr. Corbett Christie, at 210-258-9870 or cchristie@sfbr.org, or visit www.sfbr.org and click on "Support SFBR." ■

# *Southwest Foundation Forum*

I would like to thank the numerous dedicated and generous women of the Southwest Foundation Forum for another remarkable year of meeting our mission to support the Southwest Foundation for Biomedical Research through community relations, volunteer service and fund raising. I had the distinct honor of serving as the 39th president of the Forum. During my tenure, I had the pleasure of working with the most phenomenal group of spirited board members and dedicated Forum member volunteers.

*Laura Moorman*

Here are some of the many highlights of the year:

- We kicked off the fall season with a successful evening at Julian Gold in September. Our Ladies' Night Out event was a fun night of cocktails, hors d'oeuvres, and (of course) shopping; and the very generous folks at Julian Gold donated $5,000 back to the Forum!
- In October, the Forum and Founder's Council hosted an entertaining and informative Foundation Evening Tour. The Founder's Council generously provided bus transportation to and from the Foundation, and it was a completely full and energetic ride that led to a record turnout.
- In November, our Fall Lecture Luncheon was another sellout event where almost 200 women listened to Dr. Lawrence Cohen encourage them to rethink wellness and healing with the help of homeopathy.
- Many Forum members hosted numerous high school science classes on tours of the Foundation. The city's best honor and advanced placement students learn valuable lessons from the SFBR scientists and often become inspired to go on to work in the field of science.
- The new Science Award incentive plan was a success. We received a record number of applicants. The Forum and the V. H. McNutt Foundation were delighted to award six schools with cash prizes ranging from $1,000 to $7,000. Thanks to the L.D. Ormsby Foundation, even the non-winning schools enjoyed a $200 'participation' award, and eighteen teachers received a $50 gift card just for their qualifying application.
- At our Spring Lecture Luncheon, another sellout Argyle crowd learned more about the solar and wind forms of alternative energy from Amy Hardberger of the Environmental Defense Fund in Austin.
- Once again, the highlight of the year was the annual gala at the Argyle to raise seed grants for Foundation scientists to advance their research. Chair Anne Johnston, along with Cochair Anne Heaner and Gala Assistant Kim Shepperd produced the event titled Beyond the Sea, complete with gaming tables and other opportunities to support SFBR. The Forum Gala is our main fund-raising activity, and we were very appreciative of all of those who bought tables, gave direct grant donations, and helped in so many ways. This was a tough economic year for everyone, so we were especially grateful to all participants.
- The Forum is almost 600 members strong, and we are on track to maintain this number for the 2009-2010 year. We always welcome new members and promise to continue to encourage current members to renew. Joining the Forum just takes $35, and there is no obligation to volunteer, although members do have the opportunity to help as little or as much as they would like.
- All members were kept up to date with Forum activities and the latest research at SFBR via our three informative newsletters. The fall, winter, and spring issues of *Forum in Focus* may be accessed on our Web site, www.swff.org.
- The Forum's Web site has come a long way since its inception in 2004. It has been updated to meet today's needs for online commerce of all Gala-related purchases, membership, and lecture luncheons. Please check us out when you have a moment.


*SFBR Board Chair John R. Hurd accepting Gala check from Anne Johnston, Gala chair; Anne Heaner, Gala cochair; Allison Zeller, SWFF president; and Kim Shepperd, Gala assistant.*

- Forum events and photos were featured in many publications this past year including the *San Antonio Express-News*, *North San Antonio Times*, *Brilliant* magazine, *SA Woman,* and *Scene in San Antonio*.

It was a true privilege to be the president this year. My job was so easy because the board members took their responsibilities seriously and dedicated themselves to giving their all. I'm looking forward to my role as past president and want to take this opportunity to remember two of our past presidents who passed away this term. Neal Krause was our sixth president in 1975-76 and Margie Rust was our 18th president in 1987-88. They were both dedicated women and, I'm sure, would be proud to see the Forum's continued success.

I am beaming with pride to introduce to you the Forum's new president, Terry Gouger. There isn't a more dedicated human spirit on the planet, and we are so fortunate to have her. On my last day as president, Terry presented me with a beautiful bowl with an inscription of a Tom Slick quote, "I don't believe in failure, only outcome. When there is a disappointment, I never think it is the end of the story, but the beginning of something new, sometimes a great adventure." I will cherish this bowl and my time as president forever. Welcome to your new adventure, Terry!

**Laura Moorman, SWFF President 2008-2009**

# *The Argyle*

For more than 50 years, The Argyle, a stately Southern mansion and unique private club, has been devoted exclusively to the support of the life-saving efforts of the Southwest Foundation for Biomedical Research. Founded in the 1950s and located just eight miles from downtown San Antonio, the 1,400-member club serves as a bond between one of our country's leading independent research institutions and those who give time and money in support.

Originally built in 1854 as the headquarters of a horse ranch that extended from downtown San Antonio to the town of Boerne, some 30 miles distant, it was an outpost of Texas hospitality. Through a succession of owners, it epitomized the pleasant ways and good living of the storied South. It was purchased in 1884 by two Scotsmen, who added the third floor and opened a hotel. They named it The Argyle because the surrounding rolling hills reminded them of their native Scotland. It was a happy event that The Argyle came into the capable hands of the fabulous Miss Alice O'Grady around the turn of the century. The Argyle was legendary throughout the world for its fine table and illustrious guests.

In 1954, Dr. Harold Vagtborg, Southwest Foundation's first president, and Betty Slick Moorman, sister of founder Tom Slick Jr., discussed ways to interest more people in the Foundation's work and to create a broader and more permanent base of support for its research programs. Betty Moorman suggested the establishment of a high-caliber club whose members would make an annual contribution to the Southwest Foundation, and thus The Argyle of today was formed.

Restored in 1956, The Argyle stands as a symbol, both of its rich past and of progress toward a healthier tomorrow for the global community. Formed by persons deeply interested in the Southwest Foundation for Biomedical Research, the club is a meeting place for men and women of science and civic leaders who have dedicated personal resources for the advancement of the Foundation.

The Argyle is the scene of many grand occasions such as weddings and family events, as well as meetings of numerous Southwest Foundation support groups and trustees. One of the most popular initiatives is a series of "Fireside Chats," held for Argyle members and guests. This program allows members to meet with Foundation scientists in a social setting to enjoy a conversational exchange of ideas and information regarding the scientists' research efforts. In 2008, four of these popular chats were hosted. The year kicked off with an overview of SFBR programs by Dr. John L. VandeBerg. In March, Dr. Robert Shade spoke on his research into the influence of salt intake and hypertension. The fall series featured two of the Foundation's rising stars, Dr. Ricardo Carrion Jr., the manager of the maximum containment laboratory who leads research into vaccine and therapy development for devastating viruses, and Dr. Harald Göring, whose research into genetic influences on heart disease and inflammation is among the most cited in his field.

Argyle members continue to live up to their vision of honoring the past while at the same time changing the future through their philanthropic investments in the Southwest Foundation. ■

# *Credits*

The SFBR Annual Report is a publication of the Southwest Foundation for Biomedical Research.

Editor: Joseph Carey, SFBR Vice President for Public Affairs

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**Photography Credits**

File Photo: front cover, right; pages 16, 40, 51

Robert E. Lanford, Ph.D.: page 7

Qiang Shi, Ph.D.: pages 4, 27

Clem Spalding: front cover, left; pages 18, 23

Marie Tehas: page 30

Sarah Williams-Blangero, Ph.D.: front cover, middle; pages 8-10

Matthew Williams: page 11

Larry Walther: pages 13, 14, 21, 24, 28, 29, 41, 42, 45, 47, 50



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