SFBR
PROGRESS
Fall Issue 2003
A Publication of the Southwest Foundation for Biomedical Research

Targeting Terrorism

SFBR assumes larger role in biodefense

INSIDE:

President's Column

Dr. Frank F. Ledford, Jr.
President

The name of this publication is *Progress*, and appropriately so, for I cannot think of a more fitting word to describe what is happening at the Southwest Foundation for Biomedical Research. Efforts to build up our campus and build upon scientific understanding of human health and disease are advancing at a rapid pace.

This past summer, we opened the SBC Genomics Computing Center, a beautiful facility that has allowed us to expand the size of our "computer ranch" so dramatically that it can be called the world's largest computer cluster devoted to statistical genetic analyses.

Now, after major renovations, we are reopening our molecular and biochemical genetics building. To catch a glimpse of the exciting research that will take place in its 10 new laboratories, be sure to read this issue's faculty feature on Dr. Tim Anderson.

Construction crews also are moving full-steam-ahead with new housing facilities for our growing animal colony. These facilities are important for maintaining a good quality of life for these animals, something important in its own right and because happy, healthy animals are necessary for top-quality research.

Two shining examples of the value of our baboon colony are highlighted in this publication. One describes advances the Foundation is making in the care of premature infants, while another focuses on SFBR's longest-standing program, the Baboon Program Project. This spring, the project was awarded the largest grant in Foundation history, indicating its great potential to improve our understanding of heart disease.

Our Southwest National Primate Research Center, along with our scientific expertise and unique resources in the Department of Virology, are important assets to a new Regional Center of Excellence for Biodefense and Emerging Infectious Diseases, recently established by the National Institutes of Health. You can read more about this initiative beginning on page 3 of this newsletter. This feature explains how our collaboration with other academic and private research organizations is playing a key role in national defense efforts.

My thanks go out to the many donors who have contributed to our capital campaign. As you can see, your donations are allowing us to build the facilities and recruit more of the outstanding faculty that enable these advances. In fact, this issue of *Progress* features a great philanthropist, Betty Kelso, who is carrying on a family tradition of community support. We are particularly grateful for her contributions toward our new genetics facilities.

While we have come far in our capital campaign, we still have a short way to go, so we continue to look for your support in carrying out the initiatives we carefully planned several years ago. Thank you for being our partners in progress.

Newsbriefs

The Kronkosky Charitable Foundation recently awarded two $50,000 grants to SFBR for the study of type 2 diabetes, also known as adult-onset diabetes or non-insulin-dependent diabetes mellitus. One grant was awarded to Dr. Ravindranath Duggirala in the Department of Genetics to conduct further investigations related to chromosome 9, which appears to contain a gene or genes influencing susceptibility to the disease or its related phenotypes. As part of his investigation, Dr. Duggirala will assess five specific genes that are potential candidates. A second grant was awarded to Dr. Anthony Comuzzie, also in the Department of Genetics, who has developed a pilot study to validate the baboon as a unique new animal model for diabetes research. Similar to humans in genetics and physiology, baboons, too, are susceptible to the spontaneous onset of type 2 diabetes. The development of this new animal model will be useful in helping scientists find genes that influence susceptibility to diabetes, as well as in the development and evaluation of drugs to treat or prevent this serious disease.

Southwest Foundation is making great strides in its campus modernization efforts. Currently, scientists are moving into the newly renovated molecular and biochemical genetics building, which features faculty offices and 10 new state-of-the-art laboratories. This completes what is known as Phase II of SFBR's Campus Modernization Plan. Now the Foundation is gearing up for Phase III, which involves major renovations of the Slick-Urschel building complex. The area to be renovated includes 40,000 square feet of office and laboratory space for the Foundation's statistical genetics faculty and support staff as well as the Foundation's library. This fall, the National Institutes of Health awarded a $3.1 million construction grant, to be matched by institutional funds, towards this effort.

Dr. Henry McGill, senior scientist emeritus in the Department of Physiology and Medicine, was asked to address the American Heart Association at its annual meeting in Orlando, Fla., in November. As the premier cardiovascular clinical and research meeting in the world, the gathering typically draws 40,000 attendees from around the globe. Dr. McGill's presentation focused on a collaborative research project known as the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study, which brings together investigators from SFBR, the University of Texas Health Science Center at San Antonio, and a dozen other centers around the United States. Over a seven-year period, investigators with this project examined autopsy specimens of nearly 3,000 youths and young adults ages 15-34 who died of external causes, such as car accidents. Their findings revealed that, even in these young people, the well-known risk factors for adult coronary heart disease are associated with the rapid progression of coronary atherosclerosis, since subjects with one or more of those risk factors already showed a greater build-up of atherosclerotic plaques that can lead to a heart attack later in life.

PROGRESS

Editor and writer: Julie Collins, director of communications
Design and production: Jeffrey Heinke Design
Photography: Clem Spalding, Melanie Rush Davis, Joan Snow and Geno Loro

Progress is a publication of the Southwest Foundation for Biomedical Research.
If you would like to be added to our mailing list or to update your mailing information, contact Julie Collins at (210) 258-9437.

Protecting the nation

SFBR takes on expanded role in biodefense

Already a leader in research efforts to combat bioterrorism, SFBR's role in this arena has grown even larger in recent months since it was named part of a new Regional Center of Excellence for Biodefense and Emerging Infectious Diseases (RCE).

Continued on page 4

Protecting the Nation, continued from page 3

Established in September by the National Institute for Allergy and Infectious Diseases, one of the National Institutes of Health, eight new RCEs across the country are charged with the task of developing diagnostics, vaccines and treatments for possible bioterror agents and emerging diseases.

In times of national biodefense emergency, the RCEs will rapidly realign their activities to assist local response efforts within their region. This includes making their core facilities and other resources available to assist in the implementation of biodefense plans.

A new type of RCE

The NIH establishes RCEs as a way of bringing together scientists and institutions with a unique combination of expertise and resources to help solve a pressing national or world health problem. The RCE program was expanded to include centers devoted to biodefense studies following the Sept. 11, 2001, terrorist attacks and the anthrax incidents that occurred the next month.

SFBR is part of a new RCE in what the federal government describes as Region VI. Led by the University of Texas Medical Branch at Galveston (UTMB), this RCE includes a consortium of 16 collaborating institutions from Texas, Louisiana, Arkansas, Oklahoma and New Mexico.

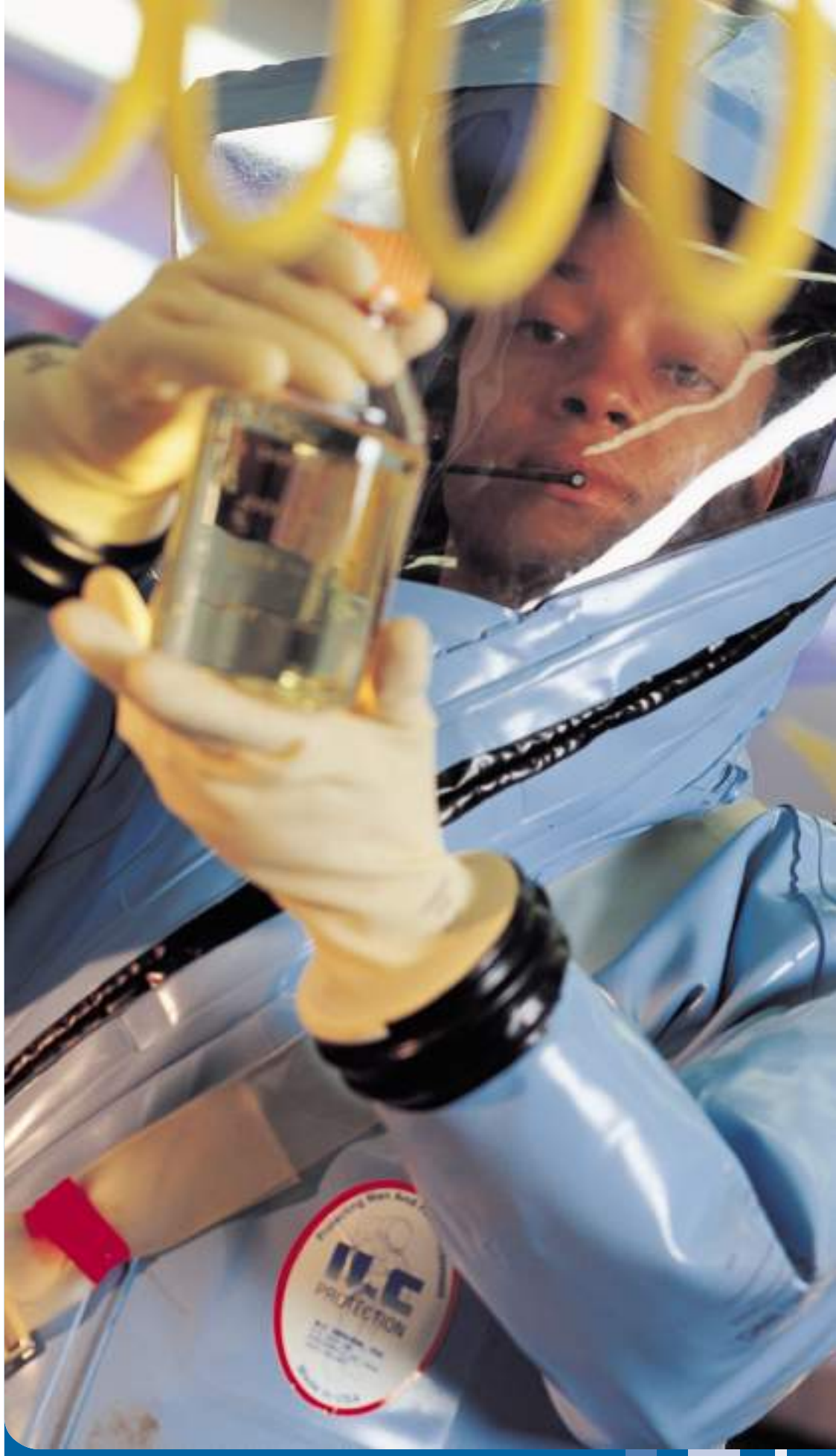
With funding provided by a $48 million grant awarded to and distributed by UTMB, these institutions will work together to study agents the government has determined to be bioterror threats, often described as "select agents." Examples include anthrax, bubonic plague, Ebola, tularensis, and viral hemorrhagic fevers. The RCE program, however, also addresses emerging infectious diseases such as dengue fever, monkeypox and SARS.

SFBR fills need no one else can

The Southwest Foundation for Biomedical Research plays a key role in the Region VI consortium by offering not only scientific expertise but also two critical resources: the nation's only privately owned biosafety level 4 (BSL-4) laboratory and the Southwest National Primate Research Center. SFBR is the only institution in the country to house both types of facilities, a benefit of particular importance to the RCE.

BSL-4 labs, also described as maximum containment laboratories, are specially equipped for the safe study of dangerous and infectious pathogens for which there is no known treatment or cure. Having such a state-of-the-art facility has allowed SFBR virologists to study select agents such as Ebola and Lassa fever since the lab "went hot" in 2000.

Already SFBR's progress in biodefense has proven



Scientists working in the BSL-4 lab hold the key to developing new treatments and vaccines against bioterror agents.

noteworthy. In June 2002, it joined the University of Texas at Austin in announcing success with a high-affinity antibody that saved lab rats from anthrax toxin. While antibiotics can kill anthrax bacteria, initial tests have shown that this new antibody can clear the body of the deadly toxins the bacteria produce. These toxins are what prove fatal in patients with late-stage anthrax infection. Funds from the RCE will support similar existing research programs at the Foundation and allow their further expansion.

"Although we have been working in the area of biodefense since we built our BSL-4 lab, the added funds from the RCE will allow us to grow significantly in this arena by expanding our antiviral therapeutic screening program," said Dr. Jean Patterson, chair of SFBR's Department of Virology and Immunology.

Another key collaborator in the RCE is SFBR's Southwest National Primate Research Center, which will provide animals, facilities and expertise to researchers developing vaccines and therapies to treat infections with select agents. The primate center's distinguished history in the humane and appropriate use of nonhuman primates in biomedical research becomes especially important in light of the FDA's "two animal rule."

"It is unethical to test the efficacy of select agent vaccines or treatments in humans," said Dr. Suzette Tardif, associate director of the primate center. "Scientists cannot, for instance, give a human a vaccine for Ebola and then challenge him or her with the virus."

For this reason, the Food and Drug Administration has ruled that new treatments and vaccines in the biodefense effort can forgo traditionally required human clinical trials if they prove safe and effective in two animals, one of which is expected to be a nonhuman primate. Because these animals' genetics and physiology are so much like our own, it is reasonable to assume that a drug that proves safe and effective with nonhuman primates will also be safe and effective in humans.

Although we have been working in the area of biodefense since we built our BSL-4 lab, the added funds from the RCE will allow us to grow significantly in this arena by expanding our antiviral therapeutic screening program.

– Dr. Jean Patterson
Chair of SFBR's Department of Virology and Immunology

Commenting on the experience and capabilities of SFBR's Virology Department and its Southwest National Primate Research Center, Dr. Frank F. Ledford Jr., SFBR president, said, "The unique combination of expertise and resources available at SFBR should prove to be a tremendous asset to the nation's biodefense effort. We are delighted with this new opportunity to expand work we already are doing, unite it with the efforts of other respected organizations in our region, and hopefully make the world a safer place for us all."

Other designated institutions

Along with UTMB and SFBR, other institutions in the Region VI consortium include the University of Texas Health Science Centers at San Antonio and at Houston; the University of Texas at San Antonio and at El Paso; Texas A&M University; Rice University; the University of Texas Southwestern Medical School at Dallas; the University of Houston; the University of Oklahoma; Louisiana State University Health Science Center at Shreveport; Tulane National Primate Research Center; the University of Arkansas; the University of New Mexico; and MacroGenics Inc., with laboratories in Dallas.

The seven other RCEs were awarded to Duke University, Harvard Medical School, the New York State Department of Health, the University of Chicago, the University of Maryland, the University of Washington, and Washington University in St. Louis.

National safety is on the minds of SFBR virologists as they go about their research in biodefense.

Premature babies could benefit from

new therapy studied at SFBR

Staff in SFBR's NICU have the unique job of caring for premature baboons.

The 500,000 infants born prematurely in the United States each year have a good chance at survival thanks to modern advances in neonatal care, including some therapies developed at the Southwest Foundation for Biomedical Research. Now SFBR researchers are testing a new therapy that could help the tiniest of infants survive and give them a better quality of life after they leave the hospital.

While nasal CPAP ("See-pap"), or continuous positive airway pressure, already is being used to treat premature infants in some other parts of the world, research at SFBR could provide the scientific data needed to support its use in the United States.

Nasal CPAP is designed to help babies with underdeveloped lungs breathe without tracheal tubes and ventilators, which can potentially inflict further lung damage. The expectation is that infants treated by this means will develop stronger, healthier lungs and be less susceptible to asthma and other breathing difficulties experienced by many children who were born prematurely.

Development and incidence of lung disease in premature infants

Premature infants have incompletely developed lungs with a reduced number of alveoli, or air sacs, which help the lungs perform their primary function of gas exchange. Many preemies also lack a natural substance in their lungs known as surfactant, which keeps the alveoli from sticking together or collapsing when the babies breath out.

Both of these factors can lead to hyaline membrane disease, also known as respiratory distress syndrome (RDS), an acute, life-threatening form of lung disease that occurs within hours after birth and necessitates artificial assistance to help the baby breathe.

Between 20 and 30 percent of babies with RDS – approximately 5,000 to 10,000 babies each year – will go on to develop a chronic lung disease known as bronchopulmonary dysplasia (BPD). Babies with BPD require assistance with breathing for an extended period of several weeks or months.

Together, BPD and RDS are responsible for most of the infant morbidity and mortality in developed countries, and

many survivors go on to have continuing breathing problems such as asthma in early childhood.

SFBR's unique resource helps save the tiniest of lives

Over the past 20 years, the Southwest Foundation for Biomedical Research has been heavily involved in the development of advances to give these babies a fighting chance, and in doing so, they have used a resource that is one-of-a-kind: a neonatal intensive care unit devoted to premature baboons. Under the direction of Dr. Jacqueline Coalson and with the assistance of Foundation scientific and veterinary staff as well as collaborators from around the globe, the program has made great strides over the years.

The quest began in the early 1980s, when some baboon mothers were delivering their babies too prematurely to survive. Trying to determine the cause of death, SFBR scientist Dr. Henry McGill examined the lungs and found evidence of lung disease. He showed the lungs to Dr. Coalson, a pathologist at the University of Texas Health Science Center at San Antonio, who confirmed that these premature monkeys did in fact have an identical lung disease to that found in human preterm babies.

That led to the development of a unique NICU at the Foundation to study the premature baboon as a natural model for lung disease in premature infants. Initially, the research group led by the late Dr. Robert deLemos studied how a ventilator injures the lung.

This understanding led SFBR researchers to refine the technique of high-frequency oscillatory ventilation (HFOV), which Dr. Coalson describes as "a gentler way of helping the baby breathe." The HFOV ventilator delivers soft, tiny breaths 600 times per minute, which is much easier on the baby's lungs than the traditional ventilator and causes less scarring of lung tissue.

Dr. Coalson says that HFOV is now a very well established and effective treatment for both preterm and term babies with severe lung problems requiring ventilation. However, she says the extended use of any ventilator puts babies at greater risk of more severe lung problems and the development of BPD. Part of the risk is the need for endotracheal tubes, which can create a passageway for bacteria that can cause infection and inflame the baby's lungs.

The continued – and promising – search for improved treatments

In their attempts to reduce the incidence of lung damage and BPD, researchers are looking for a better way of helping preemies breathe, and they think they may have found it in nasal CPAP.

"Instead of placing a tube down a baby's trachea and

Continued on page 8

At SFBR, researchers are studying new and better ways to save the tiniest of infants. Here, one premature baboon grasps the hand of its caregiver.

After successful treatment with nasal CPAP, this premature baboon is healthy and playful on what should have been his actual birthday.

Nasal CPAP, continued from page 7

forcing it to breathe the way a ventilator wants it to, with nasal CPAP we put prongs on the baby's nose that let it control its own breathing," said Dr. Merran Thomson, an adjunct scientist at SFBR who is based at Imperial College in London, England.

She explained that the nose prongs are attached to a "blender" that mixes oxygen and air, as well as to a flow meter that varies the pressure support to the baby's lungs. The air also is warmed and humidified before entering the baby's nose to prevent the delicate airways from being damaged.

The result, explains Dr. Thomson, is that "We believe nasal CPAP causes less initial damage to the lungs so that babies won't develop BPD, and if they do, it will be less severe and of a shorter duration."

Some hospitals in Europe, New Zealand, Australia and New York have been using nasal CPAP for many years. The incidence of BPD appears to be considerably lower in these hospitals than in many comparable hospitals not using nasal CPAP early in a baby's life. A medical research paper published in 2000 highlighted the differences. It looked at babies cared for in three U.S. hospitals and found that only 4 percent of those cared for with nasal CPAP from birth developed BPD compared to an incidence of 22 percent if the babies received initial help with breathing from a ventilator.

So why aren't most American hospitals using this new therapy? Besides seeming to help infants, the equipment it requires is less expensive than ventilators. In addition, the equipment is less cumbersome, allowing mothers to hold their babies earlier, and the babies do not have to be sedated, so they can be fed naturally. All of these things are known to be beneficial to the child's development.

The problem is twofold. First, nasal CPAP is more labor intensive and dependent upon skilled nurses, making it costly and difficult to implement in areas that already face nursing shortages.

The other problem – one that must be met before hospitals implement a program requiring more nursing staff – is a lack of scientific data showing that nasal CPAP is the reason for lower incidence of BPD in some parts of the world.

Local research yields encouraging results

That is what makes the research program at SFBR vital, and results so far are quite promising. Two years ago, Dr. Thomson came to the Foundation to teach its staff how to administer nasal CPAP and to see if it could be done successfully with premature baboons. They used the therapy on baboons that were born prematurely at a comparable age to human infants born three to four months too early. Later examination of the lungs showed encouraging results.

"Their lungs were in terrific shape," said Dr. Coalson. She explained that the lungs did not show the damage or infection typically seen in those premature infants who have been on a ventilator for an extended period.

Also exciting for researchers was that the baby baboons' alveoli continued to develop after birth just as they would have done inside the womb. This degree of lung development is something that has not been found in preterm infants who are ventilated for several weeks or more.

Both Dr. Coalson and Dr. Thomson agree that their findings two years ago are encouraging for the immediate and long-term health of premature infants who could be treated solely with nasal CPAP.

This past summer, Dr. Thomson was back in San Antonio leading a follow-up study to discover what happens to preemies who first need help from ventilators and are then switched to nasal CPAP for continued breathing assistance. As she and Dr. Coalson examine their research data over the coming months, they hope to confirm that the early use of nasal CPAP is a superior method of treatment for these tiny babies.

Dr. John VandeBerg looks on as Mari Hui works with samples from the Baboon Program Project.

SFBR's longest-running program awarded $14.7 million grant,

advances understanding of heart disease

The longest-running grant at the Southwest Foundation for Biomedical Research became the largest grant in the Foundation's history when the Baboon Program Project was renewed this past spring by the National Heart, Lung and Blood Institute (NHLBI) for $14.7 million over five years.

Officially titled "Diet and Genotype in Primate Atherosclerosis," the research program studies baboons to learn how diet and genes interact to determine an individual's risk of atherosclerosis, where fatty substances form deposits of plaque on the inner lining of arterial walls, contributing to heart disease.

The program aims to identify particular genes that contribute to atherosclerosis and its risk factors and then to learn how those genes function, eventually leading to the development of individually tailored diets and therapeutic drugs to help prevent and treat the disease.

The ultimate goal in all of this is to improve human health, says Dr. John VandeBerg, director of SFBR's Southwest National Primate Research Center and the grant's principal investigator. "Once we can identify a specific gene influencing a particular characteristic, we can do two things. One is to try to use that gene's mechanism of action as the basis for drug development to treat disease.

"The other thing, which we could do immediately, is to develop individually tailored dietary and lifestyle recommendations for people who carry that gene. This would help with public health efforts, because right now, for the most part, we give everyone the same recommendations, and people are less inclined to make the effort to follow them. But if we can tell someone that they have a gene that makes them highly susceptible to a particular disease and we have some specific recommendations to help offset that risk, we might be able to

Continued on page 10

Michael Torrez prepares blood samples for storage for future genetic analyses.

Heart Disease, continued from page 9

make a real impact on their lives."

Initially funded by NHLBI in 1972, the research program began operation under its current grant number in 1982, making it the Foundation's longest-running grant.

Designated by NHLBI as a program project, it actually contains multiple related research programs under one grant. These programs unite the efforts of 24 separate investigators from SFBR and collaborating institutions, all working within three major project areas. Project 1 is led by Dr. VandeBerg, Project 2 by Dr. David Rainwater and co-leader Dr. Michael Mahaney, and Project 3 by Dr. Anthony Comuzzie, all faculty in SFBR's Department of Genetics.

As one would expect, the Baboon Program Project relies heavily upon SFBR's colony of baboons, which is the largest such colony in the world. It includes a unique pedigreed colony of some 2,400 animals, for which scientists have maintained family, dietary and medical histories and complete genetic information for six generations.

The colony provides a powerful tool for genetic analyses, especially since baboons are so genetically and physiologically similar to humans, being identical in approximately 96 percent of our DNA sequence.

Making the colony even more valuable is SFBR's selective breeding program and its ability to control the animals' diet, which cannot be done with a human population. This control allows scientists to see more clearly how diet and genetics work together to influence disease.

Over the past five years, Dr. VandeBerg has seen the rate of scientific discovery through this project advance at a record pace, beginning with a milestone achievement: the mapping of the baboon genome, published by SFBR scientists in the journal *Genomics* in the year 2000. To date, it is the only gene map of a nonhuman primate.

"The baboon gene map parallels the human gene map," Dr. VandeBerg explains. "This gives us enormous new opportunities for genetic research with baboons, not only on cardiovascular disease but on many other diseases, including diabetes, obesity, osteoporosis, behavioral disorders, really any basic human disease or disorder. We can use this map to find genes that control certain characteristics, such as blood cholesterol, and from there develop new drugs and therapies to treat disease."

Since mapping the baboon genome, SFBR researchers already have identified nine chromosomal regions containing genes that influence blood pressure, blood cholesterol and adiposity, or one's degree of fat. With statistical methodologies and a novel microarray strategy developed by scientists in the program, researchers are quickly honing in on one of those specific genes, one that affects HDL, "the good" cholesterol.

Over the coming five years, they aim to pinpoint at least two more disease-influencing genes, identify new regions of the genome related to obesity and diabetes, and determine how Vitamin E interacts with genes to influence oxidative damage.

Good fortune leads to great research

The beginning of the Baboon Program Project

In the mid-1950s, SFBR scientist Dr. Nicholas T. Werthessen was visiting a research collaborator, Dr. Russell L. Holman, at the Louisiana State University Medical Center when a telephone call came through from the pathology staff at Tulane University. They had performed an autopsy on a 16-year-old baboon that had died at the Audubon Zoo in New Orleans, and they thought Drs. Holman and Werthessen would be intrigued by the results.

Sent to pick up the interesting finding was Dr. Henry C. McGill, Jr., who at the time worked with Dr. Holman and later moved to SFBR, where he became the Foundation's first scientific director and the initial principal investigator for the Baboon Program Project.

"I can remember what happened just like it was yesterday," says Dr. McGill. "I picked up the baboon's aorta and carried it back to our pathology department (at LSU) in my hot little hands on a wet paper towel. Dr. Holman and Dr. Werthessen both went ballistic when they saw it. This aorta had changes in it just like you would see in a human with atherosclerosis, which is the basis of the common heart attack. The aorta had thickened plaques on the inner lining, and some of these had yellow fat in them. This is the very hallmark of atherosclerosis."

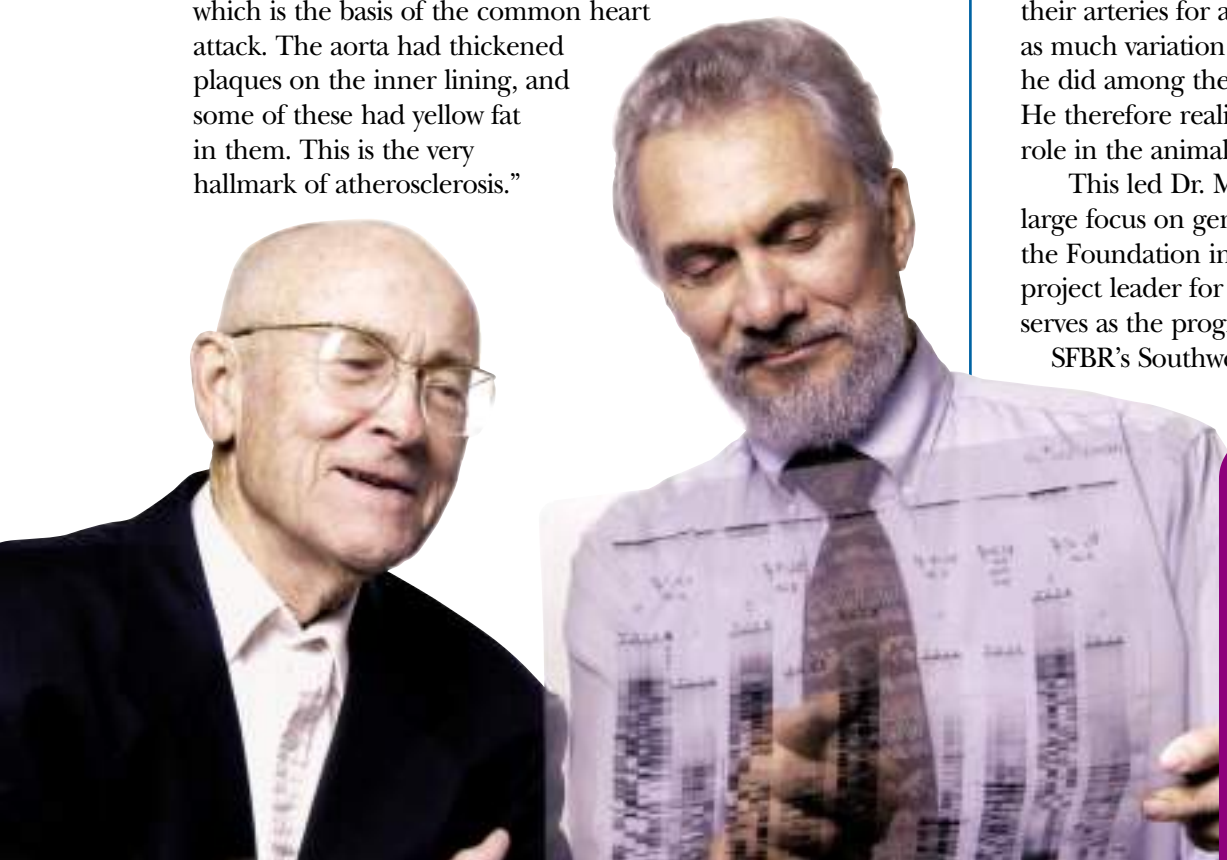
By this fortuitous observation, the researchers had found a natural animal model in which to study our nation's number one killer, heart disease. That led Dr. Werthessen to initiate the development of SFBR's baboon colony. Through his initial efforts and those of many scientists and veterinarians who followed him, the Foundation today has the world's largest colony of baboons for biomedical research. It includes a unique pedigreed colony of some 2,400 animals, on which scientists have maintained comprehensive histories for six generations. The result is an unparalleled tool in the hunt for the genes influencing disease.

Early in his career, Dr. Henry McGill, Jr. was part of a team that discovered that baboons, like people, can naturally develop atherosclerosis. Here he shows a baboon aorta with fatty plaque deposits.

The interplay of diet and genetics

It was the careful monitoring of baboons' diets that first gave SFBR researchers insight on the role of genetics in atherosclerosis. Dr. McGill fed SFBR baboons different diets. Then after a set amount of time, he examined their arteries for atherosclerotic lesions. Surprisingly, he found as much variation within groups consuming the same diet as he did among the various groups consuming different diets. He therefore realized that genetic variation was playing a large role in the animals' response to any particular diet.

This led Dr. McGill to develop a research project with a large focus on genetics. Dr. John VandeBerg was recruited to the Foundation in 1980 as its first geneticist and became a project leader for the Baboon Program Project. Today he serves as the program's principal investigator and is director of SFBR's Southwest National Primate Research Center.



Dr. John VandeBerg, principal investigator for the Baboon Program Project, confers with the program's original P.I., Dr. Henry C. McGill, Jr.

SFBR geneticist Tim Anderson looks at a few places his career has taken him.

The 'i' *in* science

Dr. Tim Anderson travels the world to stamp out parasites

One of your degrees is in parasitology and tropical medicine, and today your work focuses on parasites that cause Helminthic infection and malaria. How did you come to have such an interest in parasites that you wanted to make them you life's work?

By accident, really. After earning my undergraduate degree in zoology from Oxford, I wanted to do some fieldwork studying mammal behavior. I read about other researchers studying anteaters and other mammals in Amazonian forests by catching them, attaching balls of thread, letting them go, and then following the thread trails through the forest. They were actually trying to find the animals' nests, which contain kissing bugs that transmit Chagas

> I am in the company of very good statistical geneticists who can help me with the methods that we need for actually locating the genes that give malaria its resistance to current drugs.

disease. I thought this sounded neat and fun to do, so I arranged a trip to use this method in Papua, New Guinea, where there is a series of large rodents, or giant rats, and marsupials such as bandicoots which no one knows anything about. After that, I linked up with the people at the London School of Tropical Medicine who did the original study. Through discussions with them, I realized the important link between wild animals carrying diseases that humans get and human health. This encouraged me to follow a career path that included the study of mammal populations but in respect to their role as reservoirs of human disease. This in turn led to my interest in human disease and all things parasitic.

Much of your research is aimed at locating genes in the malaria parasite that underlie its ever-increasing resistance to anti-malarial drugs, isn't that right?

Yes, if we can find the genetic changes in malaria that give it resistance to formerly effective drugs, we can understand how to manipulate those drugs to restore their efficacy, or we can design new drugs that will be effective against a resistant strain of malaria.

Is there a sense of urgency to your work?

This research is quite urgent because drug resistance is spreading at an enormous rate. The region of Southeast Asia along the border between Thailand and Myanmar, where my program is based, is the world epicenter for anti-malarial drug resistance. Parasites there are resistant to all but one class of anti-malarials. The same situation is occurring in Africa, but it's about 10 years behind.

Why is resistance spreading so quickly?

It's simple numbers, really. After a person is first infected with one malaria parasite via a mosquito bite, the parasite multiplies so rapidly that, within four or five weeks, the number of parasites in the individual's bloodstream will likely increase to 1 trillion. With that many, there will be mutations in basically every position of the parasite genome represented in that person. Then, consider that there are 500 million cases of malaria a year in the world. With so many malaria parasites accumulating in an individual person, and with so many people being treated with anti-malarial drugs, the selective pressure is enormous. This is really evolution in action. You can watch it happen. That is why you have examples of drugs dropping from rates of 100 percent efficacy to 100 percent failure within six years.

Then you and your peers must be facing a never-ending battle.

That would seem to be the case. However, the group I work with at the Shoklo Malaria Research Unit in Thailand is on the forefront of combination therapy for malaria. If we can develop more effective drugs, or restore the efficacy of some current drugs, then treat malaria patients with a drug

Dr. Tim Anderson views newly sequenced genetic data from drug-resistant malaria parasites.

cocktail, we can stack the odds against the malaria parasite. To survive, it would basically have to generate two or three genetic mutations concurrently, and the possibilities of that are absolutely tiny.

Have there been any major advancements in the field or in your own personal research that offer hope?

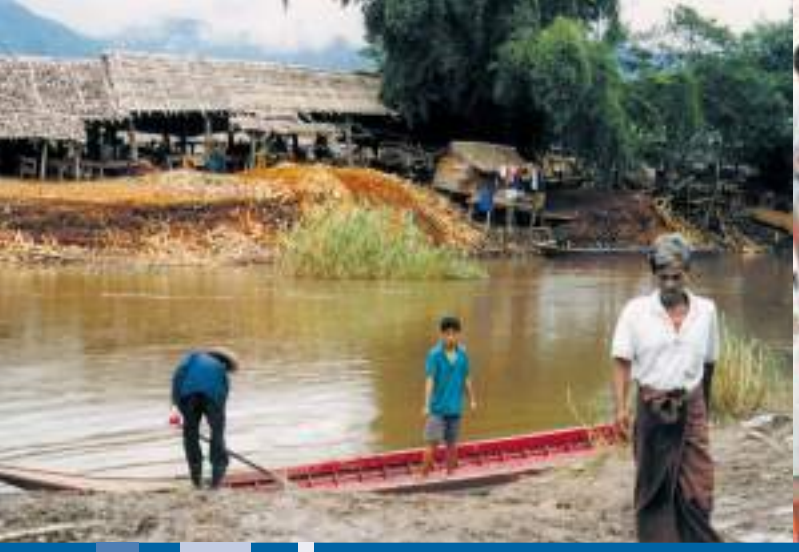
Just a year ago, an international consortium completed the genome sequence, or gene map, for the malaria parasite. So suddenly we have all sorts of genetic tools at our disposal that simply didn't exist before. Here at the Southwest Foundation, we are in a position to use that information very quickly. I am in the company of very good statistical geneticists who can help me with the methods that we need for actually locating the genes that give malaria its resistance to current drugs.

Work in our own laboratory has been encouraging as well. My research team decided to look at a gene that already is known to play a role in resistance to one important anti-malarial. What we can clearly see is a sort of scar this resistance gene left behind as it rapidly spread through the genome. This is encouraging because it tells us that we should be able to find similar scars in the genome that can help us identify other resistance genes that we don't yet know about.

We've focused on your malaria research, but it was actually your work with another parasite that led you to the Foundation. Would you describe that research and how it brought you here?

Part of my research is focused on nematode parasites, commonly referred to as roundworm. Nematode infection

Continued on page 14



Tim Anderson's research has taken him from field sites in Guatemala and Thailand to the lab bench in San Antonio.

Dr. Anderson, continued from page 13

impacts about one third of the world's population to different degrees, depending on someone's level of infection. In severe cases, it can stunt growth and cognitive development in children. There also is increasing evidence that it can cause HIV to progress to overt disease more rapidly by changing the focus of the immune system. I began studying this health problem in the early 1990s and spent a year doing fieldwork in a small Guatemalan village near El Salvador. The way this led me to Southwest Foundation is another example of a fortunate accident.

Sarah Williams-Blangero, chair of our Genetics Department, studies the genetics of Helminthic infection, which is caused by nematodes and other worms. She is trying to discover why some people in a certain village will contract just one worm while other people will be infected with 200. To find the answer, you have to study the genetics of both the parasite and the host. So, while she is studying the human genetics of Helminthic infection, she brought me in to do some work on the genetics of the nematode parasite.

Sarah e-mailed me one day while I was still working at Oxford to ask me a question about nematode biology. I believe this probably was because "Anderson" was the first name she found when she did an Internet search on nematodes and genetics through PubMed. Anyway, I e-mailed her with a response, and at the end of my note, I said, "By the way, any chance of a job?" She responded, "As a matter of fact, yes. Why don't you come for a visit?" I did. She met me at the airport, bought me a margarita, and I never looked back.

You've traveled all over the world with your research, working in Great Britain, Italy, Guatemala, New Guinea, Thailand and Nepal. Is one region of the world your favorite?

If I had to choose, I'd say Guatemala. I like Latin countries very much, maybe because I feel proud about being able to communicate, however poorly, in Spanish, but also because I enjoy their attitude toward life. It's nice to live in a foreign country where you share a sense of humor. I also very much enjoyed my fieldwork experience in Guatemala. I would get up each day around 6 a.m., have breakfast with the local policeman with gold stars in his teeth at the local shop, then walk down through the coffee groves and meet other people headed off to work. As I would go from house to house collecting samples, I would hear the local gossip, fend off psychotic dogs, and enjoy village life. Then I'd head back to my laboratory and work through the afternoon to the sound of Guatemalan pop music. It was a very nice existence. It would be wonderful to split my time now between Guatemala and San Antonio, but I'll have to wait until my children are more portable. With 3-year-old twin boys, I can be found at the Foundation or at home with my family.

You do manage to get out and play tennis, though. You've been known to arrive at the Foundation still in your tennis gear.

Yes, I do enjoy that. I used to play tennis and squash competitively when I was at university as an undergraduate, but that was a long time ago. Now tennis is a fun distraction from the pressures of worm and malaria research. I play once a week. It's my weekly humiliation at the hands of Harald Göring, another scientist in the Genetics Department.

You also still travel quite a bit, don't you? You make business trips to Thailand and Nepal, and your family travels as well.

Yes, I go off to Thailand now and then to pick up blood samples. And my wife sells antiques over the Internet, so four times a year she goes to Great Britain to buy more pieces. I'll generally go along once or twice a year to visit my family. Also, my wife is from Australia, so we go to visit her parents every couple of years. For being just 3 years old, our boys are well traveled and have racked up quite a few frequent flyer miles. In fact, they get a large number of calls from telemarketers offering them Gold Master Cards because they've taken so many flights. I have to keep handing them the phone and letting them talk to salesmen.

It sounds like you have fun with your boys. Do you have any hopes that they will turn out to be like their dad?

No, I have no preconceived ideas about what they should do when they grow up. One of them does show an aptitude for collecting all manner of insects, though, so I suppose he's off to a good start.

Betty Kelso

In the spotlight:

SFBR Trustee

Betty Kelso

Each issue of "Progress" highlights a member of SFBR's stellar Board of Trustees. In this issue, we focus on Betty Kelso. A member of the Coates family, Mrs. Kelso grew up in the ranching business, which is still a great love of hers today. In addition, she and her family have made a positive impact on San Antonio's past, present and future through their community involvement and outstanding generosity towards the arts, education, research and other important initiatives. We thank Mrs. Kelso for her years of service to SFBR, as well as for her willingness to let us share her story with our readers.

You have a long history of involvement with the Southwest Foundation, first through your mother, Elizabeth Huth Coates, who was a strong supporter, and for years on your own as a trustee and donor. What instilled your dedication to advancing research, and to SFBR in particular?

I have always believed that the work Foundation scientists are doing is incredibly important to all mankind. The diseases they are studying, their hunt for the genes that influence those diseases, and all the wonderful things they are researching are fascinating to me and will have an

Continued on page 16

Betty Kelso, continued from page 15

impact on the whole world. I love to go to Foundation board meetings and learn about their latest discoveries. I find it to be so exciting.

What, if anything, stands out for you in your years of service to the Foundation?

It's the work of the scientists that stands out in my mind, and while it all interests me, I am particularly fascinated now by studies related to genetics and, consequently, the genome. Looking back over the years, though, there are two research projects that made a big impression on me. One is the Foundation's early studies on smoking. I used to be a heavy smoker, so I followed that program very closely. I was anxious to see how my former habit would impact my children and their own inclination to smoke.

Another project I've found so fascinating is the Foundation's research with premature baboons, which can develop hyaline membrane disease and other problems that premature human infants face. I thought it was marvelous the way Foundation scientists learned about this through some natural premature births in their animal colony. Then, some of their early discoveries about how different concentrations of oxygen impact the lungs of premature infants came out right at the time Jackie Kennedy had her premature baby. It was incredible to me that research right here in San Antonio could have an impact on a health issue of such national prominence.

You mentioned your fascination with the genome, and in fact, you have been very generous to SFBR's Genetics Department. The Elizabeth Huth Coates Foundation, where you serve on the distribution committee, has funded a new genetics laboratory. Besides that, you and your husband have made personal contributions towards faculty recruitment and a new cryogenics facility to store all of the Foundation's genetic samples. Why do you think this type of research is so important?

I see so much potential in this field of research. The more we can learn about genetics, the better we will understand our predisposition to different diseases and how to offset our risk. I think this is an extremely important part of scientific understanding.

As a philanthropist who is concerned with the welfare of our community, where would you like to have the biggest impact? Your mother was dedicated to advancing the arts in San Antonio and was a driving force behind the creation of the San Antonio Museum of Art, for example. She also was committed to education and research, made evident by the fact that the Trinity University library, a research building at the Foundation, and other places of note bear her name. Do you share her same priorities, or do other goals top your list?

Certainly, mother loved the arts, she loved education, and she thought medical research was important for a multitude of people. Those were her three main interests, and they're mine, too. I particularly believe that funding of the arts is critical, especially for programs that expose children who wouldn't otherwise have the opportunity to enjoy them, because that is always the first area to get cut when there are budget deficits. Somehow, we need to work to ensure that children are exposed to the arts, which can open up whole new worlds to them. I've heard wonderful stories about people who have been inspired by a performance or by a teacher who exposed them to these things. Art can make people want to learn and see what else is in the world.

Betty Kelso appreciates how art can expose its viewers to new worlds.

You have an extensive art collection of your own. Is there one type of art or a particular artist you enjoy the most?

I love all kinds of art, from pre-Columbian to Spanish Colonial to the Impressionists and modern art, but Leon Gaspar is my favorite artist. He painted all over the world, and he caught the essence of whatever area he was in at the time, whether it was Mongolia or Russia or the Southwest.

Do you have artistic talents of your own?

I have long enjoyed painting and sculpting, which I would like to start doing again. With sculpture, for instance, it's amazing to me how you can take something like a block

of clay and make it come alive. Painting is a wonderful experience as well. To do it well, you must first learn how to see. You have to teach yourself to notice things that you ordinarily don't pay attention to, like light and shadow and negative space.

You have another love, don't you? As we speak, there are two golden Labrador retrievers lying at your feet.

I have always loved animals. I grew up on a ranch, and Bob (my husband) and I still spend half our time at ours. So I've always had animals around me – dogs, horses, cattle, wild game that we have at the ranch. We used to have an aviary as well. Now here at home we have one bird, an African grey parrot, and our two dogs, Poppy and Toffee. They're with us everywhere we go.

Your affection for animals shows through in your community involvement. Besides your support for the Humane Society, you've been on the board of the San Antonio Zoological Society and are a past president of the Exotic Wildlife Association. Most recently, you've joined a committee with the Caesar Kleberg Wildlife Research Institute at Texas A&M University-Kingsville. What does that role involve?

The Caesar Kleberg Wildlife Research Institute conducts research and activities to help conserve South Texas wildlife. This includes animals, but also native plants and grasses. So many new grasses have been introduced in Texas that they're taking over and choking out our native grasses. So I am on an advisory board that oversees interesting projects like efforts to grow native seeds and other experiments to best determine how to preserve our ecosystem. That's fascinating to me, especially as someone who has long been interested in ranch management. I'm concerned about efforts to ensure that our native plants and animals are not endangered.

With your love for animals, do you feel any conflict about supporting the Southwest Foundation for Biomedical Research, which does research with animals?

No, because I know how well the Foundation's animals are treated. I used to serve as a lay member of its Institutional Animal Care and Use Committee, which is an ethics committee that oversees all its research projects that involve animals. That was an amazing experience for me. Although I saw how lacking I was in scientific knowledge, I learned so much about how the Foundation goes about its research and cares for its animals. Knowing that and knowing how important their research is to mankind, I am proud to support the Foundation.

Speaking of things in which you take pride, your family is one. Many people have observed how important they are to you.

Oh, yes. Bob and I have five children and 13 grandchildren who range in age from 4 to 20, and we enjoy them all so much. Of course, it's hard to get together as often as we'd like since we're all scattered now among San Antonio, Austin, Houston, and Connecticut. One of my ambitions is to write my family history. Actually, that is one of many things I hope to get to someday.

You've given so much to the community over the years. Are there goals you would still like to accomplish?

There are just so many things that I would like to see come to fruition. I realize, though, that it requires more than me alone to make them happen. It takes a lot of things and the efforts of many people to turn hopes into realities. My wish is to live long enough to see more of those hopes actually come to fruition.

There are so many things I would like to see come to fruition (for our community). I realize, though, that it takes more than me alone to make them happen.

– Trustee Betty Kelso

Joining SFBR's mission to

improve human health

The Southwest Foundation for Biomedical Research would not be in its position of international leadership in biomedical research without the contributions of many corporations, foundations and individuals throughout the community.

Philanthropic partnership has played a momentous role in the Foundation's success. Unlike universities and many hospitals, SFBR cannot depend on state budget financing, patient revenue or tuition to support innovative and progressive expansion. Instead, SFBR must rely on private philanthropic investment.

SFBR researchers benefit tremendously from the contributions given by its support groups: The Golden Circle, The President's Circle, The Corporate Circle, The Founder's Council, Southwest Foundation Forum and The Argyle.

Circles of support

Members of The Golden Circle, The Corporate Circle and The President's Circle are some of SFBR's closest friends and supporters, committed to providing annual gifts of $1,000, $2,500, or $5,000, respectively, to assist SFBR in carrying out its mission. These donations are used by the Foundation to purchase new scientific equipment and other resources necessary to its scientists' valuable research projects.

To thank our partners in progress for their generosity, SFBR hosted two appreciation dinners at The Argyle this past spring. At the dinners, Dr. Sarah Williams-Blangero, chair of the SFBR Department of Genetics, presented an overview of the department's outstanding achievements during the past year.

Some of the honored guests on hand for the occasion are shown here.

The Forum's 2003 gala gave a big boost to scientific research, raising $85,000 for SFBR.

Southwest Foundation Forum

Evening in the French Quarter pays off for scientific research

For their 2003 spring gala, the ladies of the Southwest Foundation Forum chose an appropriate theme: *"Laissez les Bon Temps Roullez* (Let the Good Times Roll) – An Evening in the French Quarter."

Indeed, the good times did roll, with a turnout of nearly 500 people for a beautiful evening of games, dinner and dancing on the lawn of The Argyle. While the guests enjoyed an evening under the stars, they also helped the Forum with a highly successful fundraiser. The event generated $85,000 in proceeds to benefit SFBR.

On Aug. 20, Forum representatives met SFBR President Dr. Frank F. Ledford, Jr. at the scene of their success – The Argyle – to present their substantial donation. On hand for the occasion were Lisa Blonkvist, the Forum's 2002-2003 president; Jennifer Sparr, 2003 gala chair; and 2003 gala co-chairs Cathy Randall and Sarah Quirk.

Already, their efforts are paying off for the betterment of human health by funding three new research projects at SFBR.

Dr. David Martin received a grant for a research project that utilizes SFBR's pedigreed baboon colony to determine if there are host genetic factors that contribute to herpes infection. In humans, herpesvirus can cause disease in newborns and immuno-compromised individuals. It also is the leading cause of blindness due to infectious disease in the United States. If scientists can identify genetic contributors to this disease, they might be able to design better antivirals or an effective vaccine for herpes.

A second Forum-funded grant went to Dr. Nicolas Gouin, who is working to isolate and characterize genes important to the laboratory opossum's immune system in order to better understand the genes' role in disease susceptibility.

A final grant was awarded to Dr. Laura Cox. Utilizing two very new techniques, laser capture micro dissection and chromosomal region gene expression arrays, Dr. Cox is looking at a mapped region of baboon chromosome 5 to identify hypertension genes.

The Southwest Foundation Forum is a women's organization that works throughout the year to increase community awareness and raise funds for the Southwest Foundation for Biomedical Research. Would you like to help them make a difference? For membership information, contact Brooke Connolly at (210) 826-0260.

The Founder's Council

Anticipating the future of biomedical research

Founder's Council members turned out in large numbers for the summer lecture series.

Will doctors and scientists soon be able to "read the future" in your DNA? That was the summer topic of The Founder's Council's distinguished speaker series. On July 30, members gathered at The Argyle for a cocktail reception, followed by a presentation by SFBR geneticist Dr. John Blangero.

During his presentation, Dr. Blangero explained how scientists go about finding the genes that influence an individual's susceptibility to complex diseases. Highlighting some of the accomplishments already achieved by SFBR scientists in this area, he went on to demonstrate how future discoveries will come at a more rapid pace, thanks in large part to the completion of the new SBC Genomics Computing Center at SFBR. Featuring the world's largest computer cluster devoted to statistical genetic analyses, the center will drastically reduce the time it takes to complete complicated statistical analyses, allowing what once took months to be completed in days or even hours.

On Sept. 10, Founder's Council members gathered again, this time for a luncheon featuring Dr. Suzette Tardif, associate director of the Southwest National Primate Research Center at SFBR.

When Dr. Tardif joined the Foundation, she brought with her a colony of marmoset monkeys that, among other things, helps scientists learn about how nutrition and conditions before birth impact our health as adults.

As Dr. Tardif described her work with marmosets, she delighted the crowed with a photograph from the beginning of her career, which showed her squinting as of one of these tiny monkeys reached to pull her hair.

Events such as these are held throughout the year, geared toward individuals between the ages of 25 and 46. If you are interested in joining The Founder's Council, contact Corbett Christie, SFBR's chief development officer, at (210) 258-9870.

Considering a gift to SFBR?

Keep this in mind

Motivation and timing. These issues might not be discussed frequently, but they are important issues on the minds of anyone considering a charitable donation to SFBR or another worthy organization.

Motivation. Why do you want to give? This factor is as varied as there are individuals in the world. As a generality, many people tell us they make contributions because, as they say, "It makes me feel good." Others say that a gift to SFBR helps them realize a goal of advancing biomedical research that they could never achieve as effectively through their own initiative. It does feel good to know that your philanthropic investment joins those of others to enable research on some of life's most devastating diseases.

Timing. Are there special circumstances that influence when you might want to make a donation? Many donors consider their contributions at the year's end. Therefore, timing is especially important this year because of at least three major tax law changes. While tax implications are not typically a primary reason for making a contribution, they are an important consideration, so a few details of these three changes are offered below. Always consult your accountant or tax advisor on how these changes affect your situation.

Three major tax law changes for 2003

Lower overall tax rates. The top income tax rate has been reduced from 38.6 percent to 35 percent, which means that most taxpayers will find their tax rates reduced by an average of about 2 percent.
Dividend income reductions. In 2003, most taxpayers will find their dividends taxed at a maximum rate of 15 percent instead of the ordinary income tax rate of up to 35 percent.
Capital gains reductions. For sales of stock and some other capital gain property transacted after May 5, 2003, the top long-term capital gains tax rate is reduced from 20 percent to 15 percent.

Would you consider making a charitable gift to SFBR based on some of your 2003 tax savings? Why not become a Golden Circle or a President's Circle member today?

Here are some methods of giving to SFBR:

- Gifts of cash (Checks)
- Gifts of stock
- Gifts of real estate
- Gifts of life insurance
- Life income gifts
- Bequests

For further information on contributing to SFBR, you can contact the Chief Development Officer, Corbett Christie, at (210) 258-9870.

Southwest Foundation for Biomedical Research

Donation Form

Your tax-deductible donation will support SFBR's research programs in cancer, genetics, heart disease, infectious diseases, perinatal care, pulmonary diseases and many other areas of research. (Please type or print clearly, as donors and honorees are listed in our publications.)

I wish to make a donation to the Southwest Foundation for Biomedical Research in the amount of:

$_____ (Please enclose your check made payable to Southwest Foundation for Biomedical Research.)

My donation is for:

_____ Memorial
In memory of _____
_____ Special Occasion (Please list occasion and honoree.)
In honor of _____
_____ General Contribution

Name to be listed as the donor:

Full name _____
Street address _____
City, State, ZIP _____

Send an acknowledgement card to:

Full name _____
Mailing address _____
City, State, ZIP _____

Please mail a copy of this form with your check to:

Attention: Treasurer's Office
Southwest Foundation for Biomedical Research
P.O. Box 760549
San Antonio, TX 78245-0549

Thank you for your contribution to improve the health of humanity!

About Southwest Foundation

As one of the world's leading independent biomedical research institutions, the Southwest Foundation for Biomedical Research is advancing human health. Today, SFBR's multidisciplinary team of nearly 75 doctoral-level scientists work together on more than 175 major research projects.

Located on a 332-acre campus in San Antonio, Texas, Southwest Foundation partners with hundreds of researchers and institutions around the world, targeting advances in heart disease, diabetes, obesity, cancer, hypertension, psychiatric disorders, AIDS, hepatitis, malaria, parasitic infections and a host of other infectious diseases.

SFBR is the site of the Southwest National Primate Research Center and home to the world's largest baboon research colony. The Foundation enjoys a distinguished history in the innovative, humane and appropriate use of nonhuman primates for biomedical research.

SFBR was created through the philanthropic vision of Thomas B. Slick, Jr., in 1941, and it relies on philanthropy to sustain it today. Seventy percent of its annual budget is funded from competitive, peer-reviewed grants, while another 12 percent comes from contracts with biotechnology and pharmaceutical firms. Remaining expenses must be met by the generous contributions of foundations, corporations and individuals, as well as earnings from SFBR's permanent endowment.

Southwest Foundation for Biomedical Research is dedicated to improving human health through research on the detection, cause, prevention, cure and eradication of disease. For more information, please contact the Foundation at (210) 258-9400, or visit our website, www.sfbr.org.

advancing human health today.

Non-profit Organization
U.S. Postage
PAID
San Antonio, Texas
Permit No. 958

SFBR
Southwest Foundation for Biomedical Research

P.O. Box 760549
San Antonio, Texas 78245-0549