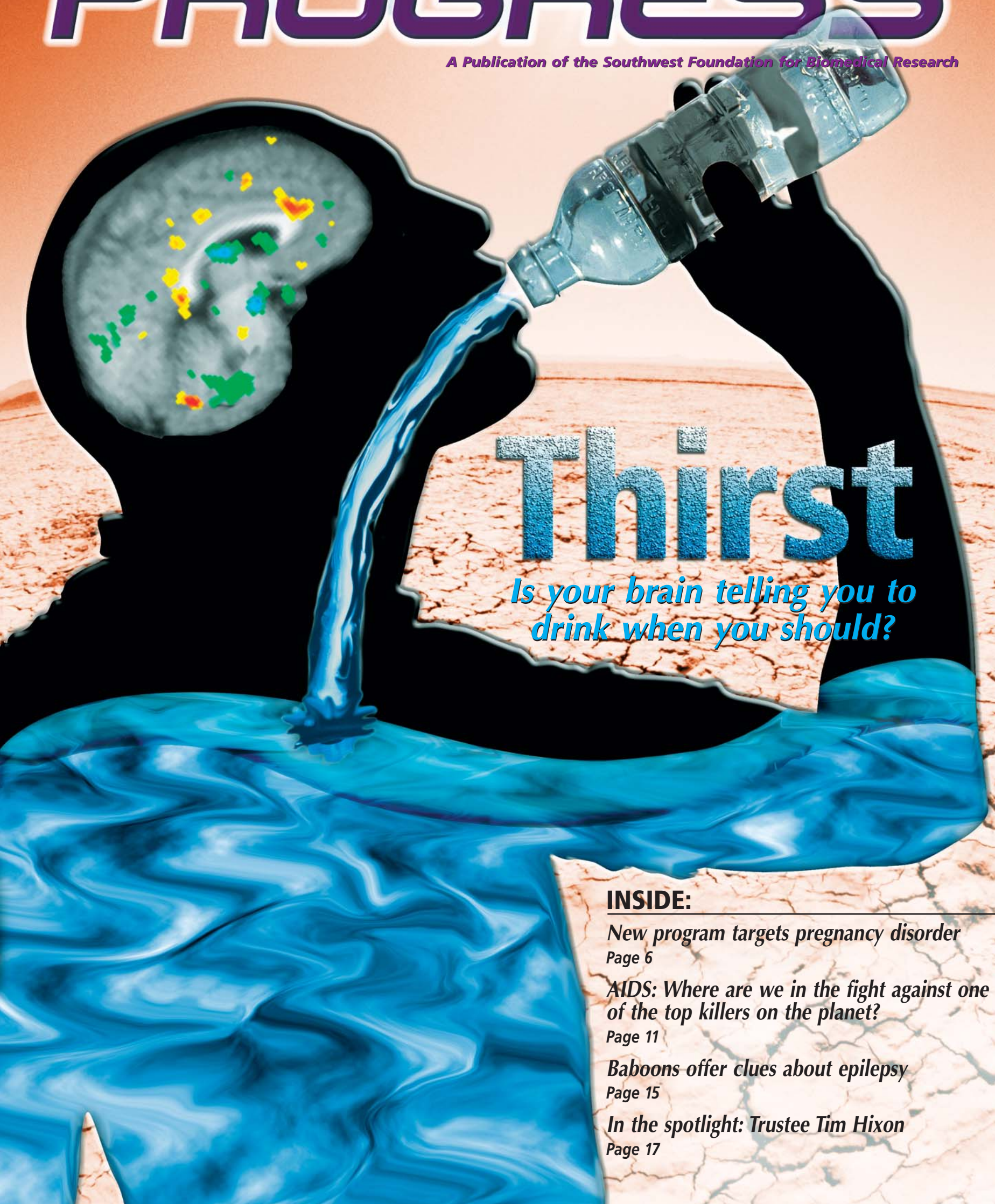


SFBR

Spring Issue 2005

PROGRESS

A Publication of the Southwest Foundation for Biomedical Research



Thirst

*Is your brain telling you to
drink when you should?*

INSIDE:

New program targets pregnancy disorder
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of the top killers on the planet?*
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President's Column

Dr. Frank F. Ledford Jr.



do you know one of the 40 million people worldwide affected by HIV, one of the 17 million people in the United States suffering from kidney disease, or one of the 2.5 million Americans with epilepsy? Since preeclampsia is the most common serious disorder of human pregnancy, chances are good that you or someone you love has been affected by this condition. And perhaps you don't even realize that as you age, your sense of thirst declines and puts you at greater risk of dehydration.

These health problems, which have local and global impact, all are under investigation by SFBR scientists. As you read this issue of *Progress*, you will learn about the unique approaches they are taking as they try to defeat these maladies.

One highlighted project is a new collaboration with the University of New Mexico to study the genetics of kidney disease in Zuni Indians, a population that is highly susceptible to this increasingly common disorder. The university asked Dr. Jean MacCluer to serve as co-investigator on this project because of her expertise in leading studies with large family groups from minority populations to uncover genetic influences on complex diseases.

The university could not have found a better partner. I recently had the privilege of promoting Dr. MacCluer to the position of senior scientist, the highest designation for a member of the SFBR faculty. In the history of our organization, this honorary title has been bestowed only upon Dr. Henry C. McGill Jr. and Dr. P.N. Rao. Dr. Thomas Butler also was honored as senior veterinarian.

Dr. MacCluer joins this distinguished group because of her exemplary scientific leadership at our institution and around the nation. While her professional credentials are outstanding, my personal admiration for Dr. MacCluer extends far beyond her abilities as a scientist. She is a special person who has positively affected many lives at this Foundation, and I congratulate her on this well deserved recognition.

This issue of *Progress* features another individual whom I hold in the highest regard, Tim Hixon. Tim was SFBR chairman when I was hired as president. As he says in this published interview, it was ironic and refreshing that Tim, who served as an enlisted Army medic in Korea in the 1960s, was later in a position to hire the surgeon general of the Army. The mutual respect we have for each other is something I treasure.

Finally, don't close the magazine without reading about the activities of our support groups. The Southwest Foundation Forum and the Founder's Council recently sponsored several exciting events, and the Golden Circle uses this issue to debut its new levels of giving to SFBR. These outstanding organizations are essential to our scientific progress. I thank their members and all who support SFBR for your contributions to human health through scientific research.

Dr. Jean MacCluer promoted to senior scientist

Congratulations to Dr. Jean MacCluer, who was recently promoted to the position of senior scientist by Dr. Frank Ledford, SFBR president, and the Foundation's Board of Trustees. Made official at the Board of Trustees meeting on Feb. 24, 2005, this appointment is the highest honor given to a member of the SFBR faculty. In the Foundation's history, the only other individuals recognized with this title have been Dr. Henry C. McGill Jr., senior scientist emeritus in the Department of Physiology and Medicine and the Foundation's first scientific director; and Dr. P.N. Rao, senior scientist and chairman of the Department of Organic Chemistry. Dr. Thomas Butler, now retired from SFBR, was honored with the title of senior veterinarian.

Dr. Ledford and the Foundation's trustees elected to honor Dr. MacCluer with this designation because of her outstanding scientific career, particularly her major contributions to the field of genetics and to the development of genetic research at SFBR.

Dr. MacCluer, who received her Ph.D. in human genetics from the University of Michigan in 1968, was the first faculty member recruited by Dr. John VandeBerg to the Department of Genetics at the Southwest Foundation for Biomedical Research in 1981. When she joined the Foundation, Dr. MacCluer was already well known as a pioneer in the application of computer methods to problems in genetic research. In her 24 years at SFBR, she has made major contributions to the field of genetics, developing an internationally recognized research program on the genetic determinants of heart disease in minority populations.

In 1982, she initiated the Genetic Analysis Workshops, and these evaluations of state-of-the-art statistical-analysis techniques have had a dramatic impact on the field of genetic epidemiology. Through these workshops, which attract statistical geneticists from throughout the world, she has fostered the career development of numerous investigators who are now leaders in the field, and she has facilitated major advances in statistical genetic methods and applications.

Dr. MacCluer has had a broad impact on biomedical research through her involvement on numerous committees at the National Institutes of Health and membership on editorial boards for the premier scientific journals in the areas of genetics and heart disease. She has also been a key figure in guiding the development of the Department of Genetics at SFBR as it has grown into a leading center for genetic studies of common diseases.

"With over 150 papers published in the scientific literature, Dr. MacCluer is clearly an outstanding researcher who continues to advance our understanding of the familial factors influencing common diseases such as heart disease, obesity, and diabetes," said Dr. Sarah Williams-Blangero, chair of the Department of Genetics. "Her research program continues to be one of the most active in our department."

To learn about Dr. MacCluer's most recent research efforts, see the article beginning on page 9, which describes a new project investigating the genetics of kidney disease in Zuni Indians.



PROGRESS

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Lost sense of thirst puts elderly at greater risk for dehydration

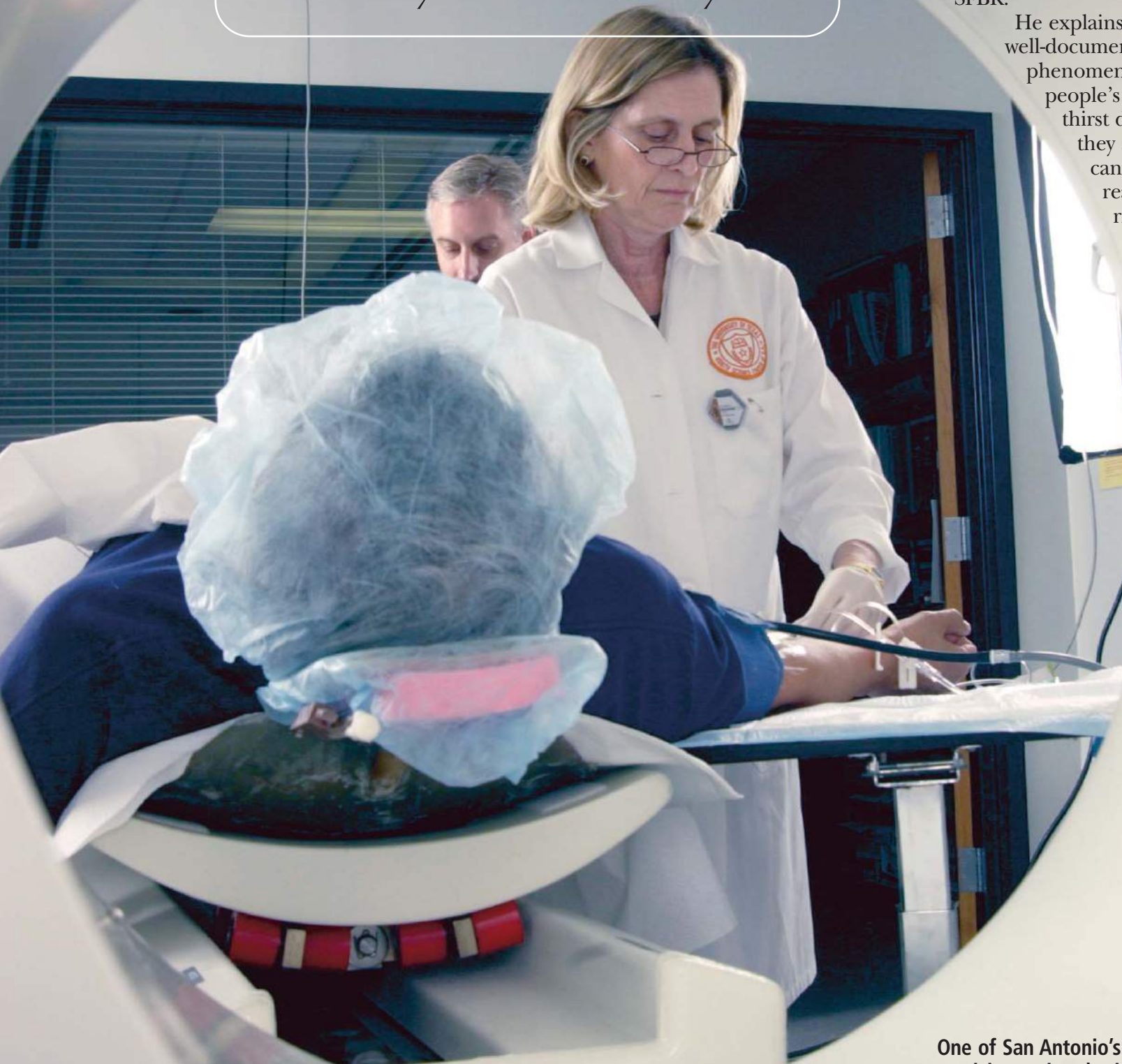
Researchers use brain-imaging study to find out why



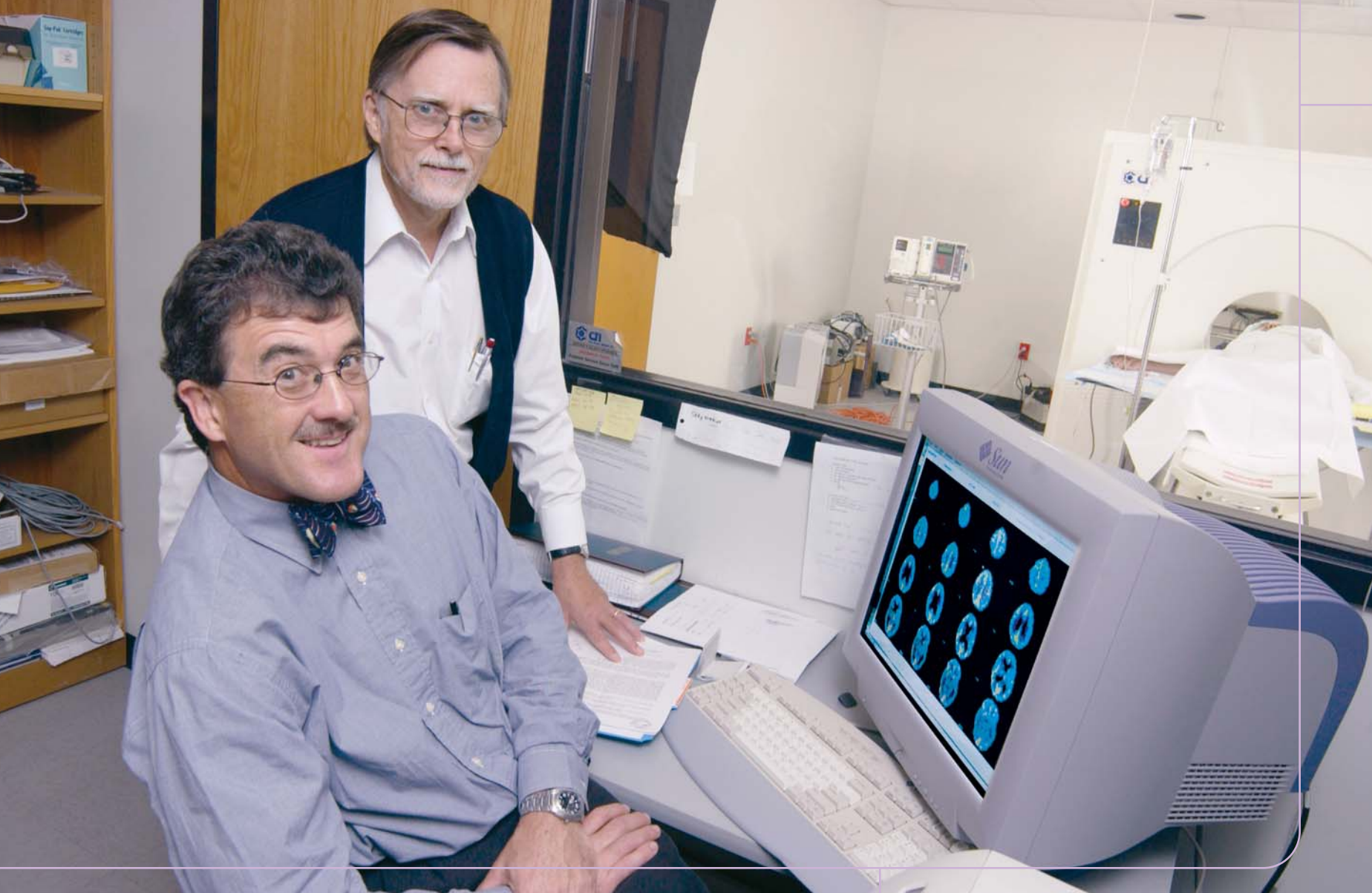
As the lazy—and hot—days of summer roll around in South Texas, senior citizens should take special care to make sure they are drinking enough water, even if they do not feel thirsty, cautions Dr. Robert Shade, associate scientific director and chair of the Department of Physiology and Medicine at SFBR.

He explains that it is a well-documented phenomenon that people's sense of thirst declines as they age, which can pose a real health risk for the elderly.

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One of San Antonio's seniors participates in a brain-imaging study to help scientists discover why our sense of thirst declines with age.



Drs. Robert Shade (standing) and Peter Fox examine brain images from a research subject's PET scan.

Thirst, continued from page 3

"Many elderly people should feel thirsty, but they don't, and because they're not thirsty, they don't drink enough liquids," Dr. Shade said. "As a result, they can become volume depleted or dehydrated."

He said that may be one significant reason why the elderly are more adversely affected by heat stress, which can send many to the hospital for emergency medical care and even lead to death, as was seen in the summer 2003 heat wave in France that killed thousands.

Wanting to offer people more than advice to be careful about drinking enough water, Shade is involved in a collaborative research project to help uncover why our sense of thirst wanes with age. If the cause of the phenomenon can be better understood, scientists and physicians might be able to find treatments to correct it.

Currently, the cause is a mystery. One suggested explanation is a "cognitive disconnect." As cognitive function declines with aging, it may be that something goes awry in the process of how a physical stimulus sends a signal to the brain and the brain interprets that signal to elicit the appropriate response. But where does that disconnect occur? And what exactly is causing it? That still needs to be determined.

"Clearly, either many elderly people are not aware of

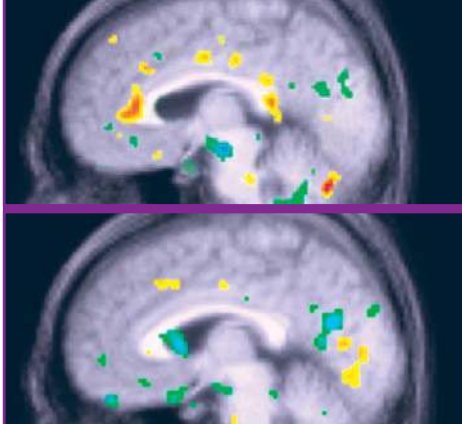
being thirsty — at least not to the degree they should be — or if they are aware of it, it isn't registering correctly and they're misinterpreting the symptoms," said Dr. Peter Fox, director of the Research Imaging Center at the University of Texas Health Science Center at San Antonio. "Perhaps they're uncomfortable, but they can't put their finger on why. So it's not clear what exactly is going on, but it is clear that when you lose the urgency of your thirst drive, you die. So this is a big risk."

Drs. Fox and Shade are working with Dr. Derek A. Denton, emeritus research professor and emeritus director, the Howard Florey Institute for Experimental Physiology and Medicine, The University of Melbourne, Australia. A grant to the Florey Institute from the G. Harold and Leila Y. Mathers Charitable Foundation, New York, is funding their investigation on thirst.

For 15 years, Shade and Denton have collaborated on animal studies exploring the physiology of salt-and-water metabolism and salt-and-water appetite. In 1997, they teamed up with Fox because of his resources and expertise in brain imaging as well as his understanding of the brain mechanisms of physiology and cognition. This combination of expertise and resources has put these researchers in a unique position to explore the physiological interaction of cerebral function and the autonomic nervous system, particularly as it relates to thirst.

The research team began its investigation by conducting several studies of a “normal” population, looking at healthy, young adults who agreed to undergo positron emission tomography, commonly known as PET scans, of their brains while experiencing different levels of thirst. These studies served to document which areas of the brain are activated as the need for fluids increases and decreases; the strength of brain signals and their reception in areas of the brain related to perception, attention and cognition; and which areas of the brain are affected by either thirst, physical stress, or both.

With the data from younger adults in hand, the investigators recruited an equal number of healthy senior citizens, age 65 and up, to participate in the same study. The thirst-challenge tests and accompanying PET scans with these older research subjects are currently ongoing. Once completed, researchers will compare the two sets of data, which they hope will help



These brain images, taken of a young adult at “maximum thirst” and after he has consumed enough water to be completely hydrated, will be compared to brain images of older adults in the same situations. Comparisons of the two groups should help researchers discover changes in brain signaling mechanisms that affect our sense of thirst as we age.

them identify parts of the thirst-signaling mechanism that are not working properly in the elderly.

“We’re going to look at where in the brain signals are getting lost as the brain first receives a signal from a thirst stimulus, then transfers that signal to the area of the brain where consciousness lies,” said Shade. “We also will look at differences in the degree of brain activation in the elderly as compared to young people. Perhaps we’ll see that the right areas of the brain are activated in the elderly, but the degree of that activation is less. That would be very informative. It would give us a clue to where the differences lie and what the problem is.”

From there, researchers expect that follow-up studies in animals will be needed to learn more about the physiological factors causing the breakdowns in the thirst mechanism, as well as how to design treatments to correct that breakdown.

Dr. Michael Farrel asks a study participant how thirsty he feels before performing another in a series of PET scans that are part of this thirst-challenge study.





Move from 'LAND DOWN UNDER' helps unravel mysteries of preeclampsia

*SFBR resources
key to tackling
the most common
serious disorder of
human pregnancy*



reeclampsia — toxemia during pregnancy characterized by the new onset of high blood pressure and other systemic dysfunction — is the most common serious disorder of human pregnancy and a

major cause of preterm deliveries, yet little is known about its cause. That, in turn, leaves doctors and expectant mothers with few options for prevention and treatment of the disorder.

Dr. Eric Moses is working to change that. Recently, he decided his best opportunity for success was to leave his post as head of the Pregnancy Research Center at Royal Women's Hospital in Melbourne, Australia, and move to San Antonio and the Southwest Foundation for Biomedical Research.

"While there is still so much we don't know about preeclampsia, we do know that [a person's] genetics is probably the single greatest risk factor. So coming here to work side-by-side with one of the top statistical genetics groups in the world will allow me



**The Foundation is one of
the few places in the world
where this work can be
done efficiently.**

– Dr. Eric Moses



Dr. Eric Moses

to accelerate my research and hopefully deliver some answers [to this problem] as soon as possible,” Moses said.

About preeclampsia

Preeclampsia affects approximately 6 percent of all pregnancies and typically sets in midway through gestation, or around 20 weeks. In severe cases, or if left untreated, it can advance to eclampsia, which is characterized by seizures, severe agitation and unconsciousness and is capable of killing both mother and child.

Moses explained that the only protective measures available involve treating the symptoms of the disorder, including bed rest and anti-hypertensive medication to lower blood pressure. However, if the condition continues to worsen, doctors are forced to deliver the baby early by cesarean section.

“Following delivery, the mother typically fares very well and quickly returns to a normal hypertensive state,” said Moses. “The welfare of the baby depends on its gestational age. The infant would face the same problems seen with premature birth, such as underdeveloped lungs, possibly coupled with growth restriction caused by preeclampsia.”

While doctors and researchers are unclear about what, exactly, brings on preeclampsia, Moses says, “The best evidence indicates that something doesn’t go quite right early in the pregnancy to establish a properly functioning placenta.” In particular, maternal arteries that supply blood to the growing pregnancy are insufficiently modified and therefore unable to provide the “incredible blood flow that is needed to sustain and nourish the growing baby. The thinking is that this ischemic state, coupled with the resulting insufficient supply of oxygen, leads to a disturbance in the placenta. And as the malfunctioning placenta tries to compensate, it releases factors into the maternal blood stream that cause a widespread disturbance of the maternal system,” he said.

Looking for answers

What Moses is asking in his research is, “What is going on between the mother and fetus early in the pregnancy that causes this malfunction? What is causing susceptibility to this disorder?” He said no one knows the answer to these

questions, but he believes the key to answering them lies in the fact that preeclampsia is highly heritable, meaning it runs in families.

Working with patients at Royal Women’s Hospital in Melbourne — the largest women’s hospital in Australia, with 5,000 deliveries per year — Moses and his colleagues have collected a study group of nearly 500 individuals from more than 50 families affected by preeclampsia. “These families form two- or three-generation pedigrees in which a woman, her mother, and her grandmother all have had preeclampsia, for example,” Moses explained.

Moses already has conducted genome scans on the individuals in 34 of those families, looking at all the genes on these individuals’ chromosomes in search of shared genetic markers, or particular sections of DNA, that correlate with susceptibility to preeclampsia. When there is strong, statistically significant evidence that something in a particular region of DNA is linked to that susceptibility, scientists have found what they call a genetic linkage signal, and Moses has found a strong signal upon a particular section of chromosome 2.

Thousands of genes lie along chromosome 2, and while in Australia, Moses and his colleagues were able to narrow their search to a 200- to 300-gene stretch. A great deal of work remains, however, in narrowing that down even further to identify the specific gene or genes in that section that influence susceptibility to preeclampsia. For this work, Moses decided his best advantage would involve moving to San Antonio and joining the faculty at Southwest Foundation for Biomedical Research.

Getting help from the extraordinary genetic resources at SFBR

He moved here in January, and while he still collaborates with his colleagues in Australia, he has teamed up with Dr. John Blangero, a statistical geneticist from SFBR whom he met in 1997, when Blangero helped teach an intensive course at Oxford University on the use of statistical genetics to study complex human diseases.

“When you’re searching entire genomes of large family groups, the data you’re generating is so enormous that some

Continued on page 8



Dr. Eric Moses meets with Dr. John Blangero in the "computer ranch" room of the SBC Genomics Computing Center. Moses says the opportunity to work closely with SFBR's renowned statistical genetics group and to utilize the Foundation's extraordinary resources for genetic analysis should lead to significant advances in his research on preeclampsia.

genes within that region, other genetic methods are helping him prioritize which of those 120 genes he should examine first.

"For example, we've used bioinformatics tools to examine that DNA interval more closely. [These methods provide] a very efficient way of going through public databases that already exist to help identify candidate genes," Moses explained. "We've also been taking human tissue obtained from preeclamptic and non-preeclamptic women at the time of delivery and then studying that tissue to

search for differences in how genes are being differentially expressed, or turned off or on."

He said that in both cases, the same individual genes "got the highest score," or showed the most relevance, "so we're building up a convincing argument for focusing on some particular genes in a very involved way."

His confidence in finding genes that influence preeclampsia along chromosome 2 is bolstered by findings by researchers in Iceland that point to this same region. He says he is encouraged that similar findings are being achieved by the few groups in the world utilizing this genome scanning approach to find preeclampsia genes. "This is further evidence that we're on the right track," he said.

That offers hope to mothers and babies worldwide. "Our aim is to find some genetic variant or gene showing a strong association with risk [for preeclampsia]. Once we do that, we should be able to develop very quickly a test for susceptibility, which would allow obstetricians to better manage a woman's pregnancy from the very start," Moses said.

He added that having an identified genetic risk factor might also point the way to new therapeutic interventions. "Knowing what the gene is and what it does might point the way to something that can be manipulated with a treatment already on the market. Hopefully, it also might lead to new methods of intervention."

Preeclampsia, continued from page 7

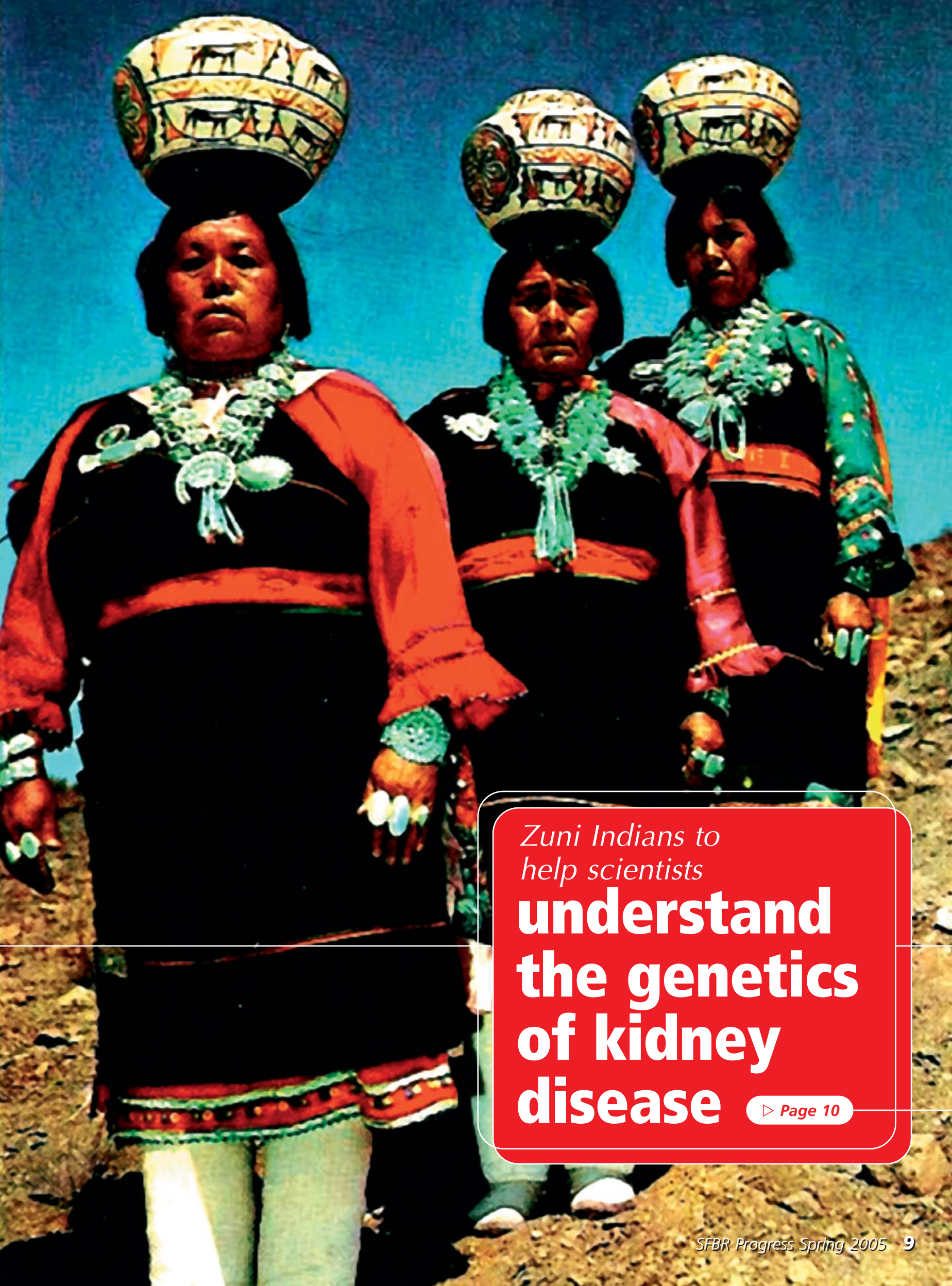
statistical genetics methods available have to drop some of that data in order to handle [the genetic analysis]," said Moses. "But John, in particular, has written statistical methods and computer software that can handle this data and give you good information on the likelihood that what you've found is relevant.

"At the same time, the Foundation has the computing capability to crunch all this data," he said, referring to the SBC Genomics Computing Center at SFBR. This facility houses the world's largest computer cluster for statistical genetic analysis. "So the Foundation is one of the few places in the world where this work can be done efficiently."

Moses added that SFBR's state-of-the-art genetic laboratory equipment, such as the latest high throughput — or super fast — DNA sequencer also helps make his research more efficient and cost-effective.

Narrowing the search

In Moses' short time at SFBR, he already has made great progress. Data crunching in the SBC Genomics Computing Center has helped him narrow that 200- to 300-gene stretch of DNA on chromosome 2 down to a shorter section of 120 genes. As he prepares to begin intense studies on particular



*Zuni Indians to
help scientists*

understand the genetics of kidney disease

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“

Our work with the Zunis could help us understand the genetics of kidney disease in the broader population.

— Dr. Jean MacCluer

SFBR senior scientist serving as co-principal investigator on a new study with the Zuni Pueblo



Researchers from the Southwest Foundation for Biomedical Research are involved in a new study in New Mexico that could have implications for improving the health of people in the Southwest. SFBR has formed a partnership with the University of New Mexico and the Zuni Pueblo to study the genetics of kidney disease among the Zuni Indians. American Indians, like Hispanics, are three times as likely as Caucasians to suffer from kidney disease, a common correlate of diabetes.

The University of New Mexico and SFBR are working with the Zunis in particular because they are even more highly disposed to kidney disease than other American Indian groups. From this study, researchers are hoping to find genes that predispose Zunis to kidney disease, and then determine whether those same genes contribute to the disease in other ethnic groups or the population at large. Identification of such disease-influencing genes could lead to new methods of prevention and treatment.

The study, funded by a grant from the National Institutes of Health, will focus on the genetics of diabetic nephropathy (kidney disease), as well as non-diabetic nephropathy. Dr. Philip Zager of the University of New Mexico is the grant's principal investigator, with SFBR's Dr. Jean MacCluer serving as a co-principal investigator. The University of New Mexico has been working with the Zuni tribe for a number of years on other research projects, and Dr. Zager said, "I asked Dr. MacCluer's group at SFBR to collaborate on this project because of their expertise and experience conducting federally funded studies designed to identify genes that modulate the susceptibility to chronic disease among minority populations."

MacCluer is involved in three other major genetics-based research projects on heart disease, diabetes and obesity in Mexican American, American Indian and Alaskan Eskimo populations.

"The Zunis of western New Mexico are particularly hard-hit by kidney disease, and we are looking for the gene or genes that predispose the population to nephropathy," said MacCluer. "It could be that we find genes in the Zunis that differ from the genes present in other populations. However, it is also possible that the same gene or genes that are responsible for kidney disease in the Zunis affect other populations as well, but it's simply easier for us to find them in the Zunis than in another population where kidney disease is less frequent. In that case, our work with the Zunis could help us understand the genetics of kidney disease in the broader population."

MacCluer explained that the study will include an effort to determine whether the same genes or different genes are related to predisposition to diabetic and non-diabetic kidney disease.

"Since there are some people who have both diabetes and kidney disease, and others who have kidney disease without diabetes, we don't know whether the same gene or genes are causing susceptibility to both diseases, or whether those diseases are influenced by different genes altogether," she said. "That's something we want to find out."

The study will include 1,000 adults out of a community of approximately 10,000 in far western New Mexico. MacCluer said the researchers will look for affected individuals who have at least one brother or sister with kidney disease.

Explaining the potential payoff of this genetic study, she added, "If you find a gene that contributes to susceptibility to kidney disease and learn how it causes the disease to develop, you might then be able to develop a way of countering the action of that gene. In other words, you could use the information about what that gene does to develop a new medication or treatment for kidney disease."

Some facts about kidney disease:

- Diabetes and hypertension are the No. 1 and No. 2 causes of kidney disease.
- The United States has the world's highest incidence of kidney disease, with 17 million Americans chronically affected.
- Minorities suffer the most, with African-Americans four times more likely and Hispanics and American Indians three times more likely than Caucasians to have kidney disease.
- The number of people in the United States with kidney disease is rising by 7 percent per year and is expected to increase by 165 percent by 2050 if current trends continue, due to this country's rising elderly and minority populations.

Source: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases



AIDS

Where are we in the fight against one of the top killers on the planet?



describing scientists' quest to discover a successful AIDS vaccine, Dr. Emilio Emini compared it to Christopher Columbus' voyage across the Atlantic

Ocean in 1492. "Until the guy at the top of the ship yelled, 'Land! Land!' he [Christopher Columbus] didn't know where he was. We [in the scientific community] are in the same situation. For all we know, we're a day away from somebody yelling, 'Land! Land!' or we still have months to go. But what if Columbus had turned around when he was only a day away? Like him, we have to keep moving forward."

Dr. Emini, a globally recognized expert on AIDS and vaccine development who works with the International AIDS Vaccine Initiative, was keynote speaker at the 22nd Annual Symposium on Nonhuman Primate Models for AIDS, held in San Antonio this past November. Hosted by SFBR's Southwest National Primate Research Center, the symposium drew researchers from across the United States and overseas to discuss the challenges and most recent scientific advances in this important effort.

20-year struggle against a deadly virus

First identified in 1983, HIV, the virus that causes AIDS, has proven to be a formidable adversary. Despite advances in its treatment, a vaccine has remained elusive, and new infections are on the rise. According to the World Health Organization, HIV infects approximately 40 million people worldwide, and there are nearly 5 million new infections each year. In the United States, 1 million people were living with the disease in 2004, up from 950,000 in 2003.

"Around the world, there are 14,000 new infections every day," said Emini, and every 10 seconds, someone dies from AIDS. "That means we're dealing with one of the largest killers on the planet. Therefore, the effort to develop vaccines to prevent the spread of the disease is very important."

He said one of the greatest

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AIDS, continued from page 11

challenges lies in the genetic diversity of the virus, which mutates frequently. That genetic variability increases the difficulty of developing a vaccine that would be effective against all subtypes of the virus. "But perhaps the greatest challenge is that we still have an insufficient understanding of the pathogenesis of the virus, of how the virus interacts with the immune system," he said.

SFBR scientists making progress

The three-day symposium allowed scientists to report on their most recent progress in overcoming those challenges. Several sessions highlighted the latest findings of scientists at SFBR.

Dr. Jon Allan: How African green monkeys "make peace" with the virus.

African nonhuman primates, unlike nonhuman primates of Asian origin or humans, are natural hosts for AIDS viruses, showing an innate ability to harbor the viruses without harm to their immune system. Chimpanzees can carry HIV, and African monkeys can carry its simian version, SIV, without developing AIDS. Part of the reason, explains Dr. Allan, seems to lie in their limited immune response.

"In humans and in monkeys that are not natural hosts for the virus, you see an overzealous immune response to infection," he said. "The immune cells targeted by HIV and SIV essentially call in neighboring cells [to help them], and as a result, more cells get infected and killed. In addition, you see collateral damage among nearby uninfected cells that are killed as part of the battle. This makes the immune

Featured Scientists



Dr. Jon Allan:
How African
green monkeys
"make peace"
with the virus



**Dr. Luis
Giavedoni:**
Identifying
"correlates of
protection"



Dr. Paul Zhou:
Finding a
new way to
fight HIV



system work very hard as it continually tries to replenish the large number of lost cells, and over time, it wears itself out.”

In African primates such as the African green monkeys Allan studies at SFBR, the opposite occurs. “They exert a more limited immune response in the beginning, which sets the stage for less viral replication and less cell killing,” he said. “Essentially, they appear to make peace with the virus rather than war, and by doing so, they limit the capacity of the virus to destroy the immune system.”

At the AIDS symposium, Allan shared his most recent findings about how African green monkeys are able to limit their immune response to SIV. After comparing tissues from naturally infected African green monkeys, uninfected African green monkeys, and uninfected pigtail macaques — a type of monkey that does progress to AIDS following SIV infection — he discovered that African green monkeys naturally have

fewer SIV target cells to begin with — five to 10 times fewer than pigtail macaques.

“Since African green monkeys naturally have fewer of the cells that SIV targets, you would hypothesize that, when they do get infected, their immune response will be muted because they have fewer cells that can be infected and therefore a lower number of cells being killed,” Allan explained.

Another thing Allan observed is that, not only do the African green monkeys have fewer target cells, but many of those target cells are able to pull in their receptors that would allow SIV to enter the cell. “When we stimulated the African green monkey cells in tissue culture, the cells down-regulated their receptors, making them less susceptible to infection,” he said.

Now one of the questions is, how can the human immune system be stimulated to respond in the same manner?

Dr. Luis Giavedoni: Identifying “correlates of protection.”

Dr. Luis Giavedoni, an SFBR scientist who chaired the local organizing committee for the symposium, studies SIV in rhesus macaques, an important model for testing candidate vaccines before human trials. To date, the most effective candidate vaccines in this model have been live-attenuated vaccines, which consist of viruses that have been weakened by genetic manipulation to the point that they are still infectious but do not induce disease. However, these vaccines are not yet appropriate for human use because of complications they have shown years after infection.

Dr. Giavedoni’s laboratory is trying to identify the type of protective immune responses induced by these live-attenuated vaccines so that scientists can design safer vaccines that induce the same protective immune responses without the complications.

In this effort, Giavedoni and his research team observed the immune responses of both vaccinated and non-vaccinated rhesus monkeys that were challenged with SIV. As Vida Hodara in his laboratory reported at the AIDS symposium, they observed both the innate and adaptive immune responses. The innate immune response is the body’s first response to infection and utilizes immune cells pre-programmed by the body’s genome. These cells do not change in response to different types of infections. Based on signals sent by the innate immune system, the adaptive immune system exerts the body’s secondary, specialized immune response. Novel antibodies are sent out to try to neutralize the infecting virus or bacteria, and novel “killer” immune cells are made to destroy cells in the body that have become infected.

One observation Giavedoni’s group made was that the vaccinated animals exerted a quicker but limited innate immune response compared to the unvaccinated animals, resulting in lower levels of inflammation. Another difference among the vaccinated animals was an increase in a chemokine called MIP-1 β , a protein produced by cells of the innate immune system that competes with some viruses for



Dr. Jeff Rogers:
Mapping the
rhesus genome

Continued on page 14

immune cells' co-receptors. HIV and SIV need these co-receptors to enter and infect the cell.

With the animals' adaptive immune response, the vaccinated animals also showed a lack of an increased antibody response. Here, the main immune response was cell-mediated. Cytotoxic lymphocytes were quickly sent out to kill SIV-infected cells.

"Based on these observations, we know that a successful vaccine needs to induce a rapid but subdued immune response that produces chemokines like MIP-1 β as well as cellular immunity," said Giavedoni, "but these findings are preliminary. We cannot yet say how to achieve that effect, and we realize that other factors in the immune response might be at play that we didn't identify. So there is still much to explore."

Dr. Paul Zhou: Finding a new way to fight HIV. Dr. Paul Zhou may have developed a new weapon in the war against HIV by taking an antibody that previously appeared to be ineffective and training it to fight in a better way.

This particular antibody is produced by the human immune system to work against part of the HIV virus known as gp41. Gp41 is a glycoprotein on HIV's coating structure that helps it bind and fuse with target immune cells. In its normal function outside the immune cell, this antibody can bind to gp41, but it is ineffective in disrupting HIV's ability to enter and infect the cell.

Dr. Zhou was still interested in this antibody, however, because of some important characteristics: it is a human antibody; it binds tightly to HIV; and it works against an epitope, or viral structure, found in many genetic subtypes of HIV. "So it could be useful against many different subtypes of the virus," Zhou said.

At the AIDS symposium, Zhou explained how he genetically engineered the antibody to express, or act, on the cell surface as part of some novel receptor molecules he developed. He designed these chimeric receptor molecules to be incorporated into the cell receptor complex that HIV uses to enter targeted immune cells.

"When expressed on the cell surface, the antibody was highly effective in blocking viral-cell fusion," said Zhou. "HIV could still bind to the cells, but it could not complete the fusion process necessary to infect those cells. By our testing methods, the cells appeared to be completely protected."

As an intermediate step to testing this as a possible therapy in humans, Zhou performed tests with cells from human tissue, called primary cells. Unlike cell lines developed in the laboratory, it is possible to infuse primary

cells back into a patient.

Zhou used an antiviral vector to deliver the gene that encodes the improved antibody to the cells. In other words, he took a virus that was genetically altered so that it can still infect cells but not induce disease, and he gave the virus this gene. That virus in turn infected the cells and expressed the antibody on the cells' surface. Once again, the cells showed protection from HIV.

"The hope is that this process could eventually be used as a genetic therapy," said Zhou. "Immune cells could be removed from an HIV patient, treated with this therapy, propagated in the laboratory, and then infused into the patient. Hopefully these protected cells would continue to propagate and eventually outnumber the person's

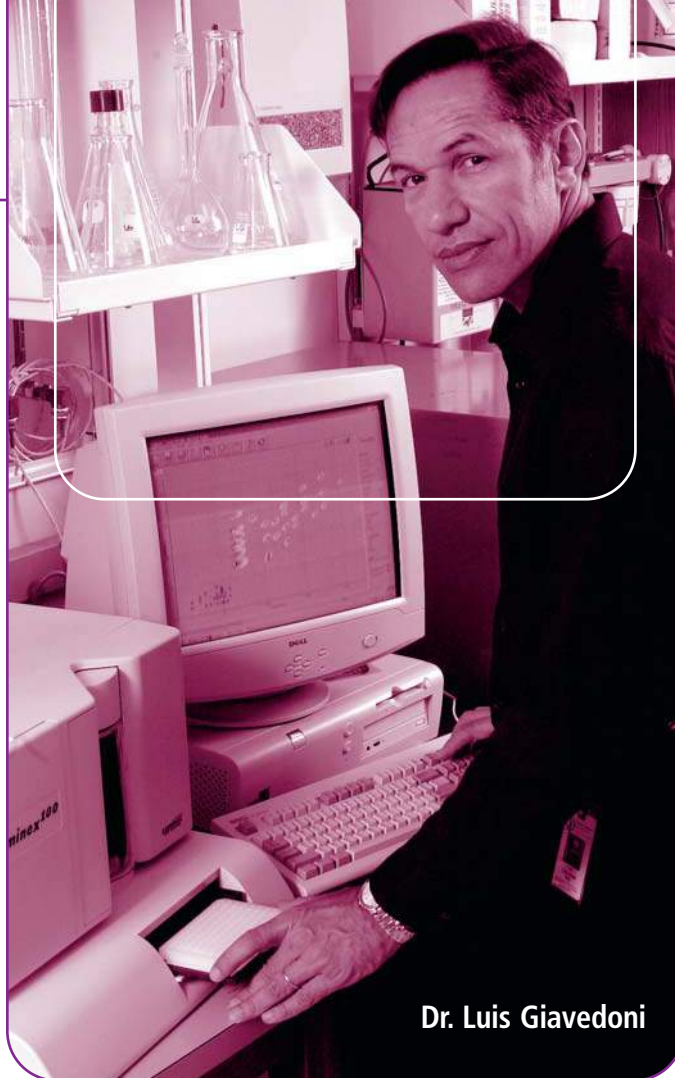
susceptible cells and thereby protect the immune system. But besides continued research that needs to be done with this antibody, there are still a lot of questions regarding how to use this type of genetic therapy safely. So much work remains."

Dr. Jeff Rogers: Mapping the rhesus genome. Though not an AIDS researcher, Dr. Jeff Rogers in the SFBR Department of Genetics reported on a project that might soon benefit AIDS investigators. He leads an effort funded by the National Center for Research Resources and the NIH Office of AIDS Research to map the genome of the rhesus monkey — the most commonly used animal model for AIDS research — and he and his research team are preparing to publish the first generation of that map.


This follows previous efforts he led at SFBR to map the baboon genome, published in August 2000 as the first genetic linkage map for any nonhuman primate.

To construct the rhesus gene map, Dr. Rogers and his team have studied DNA samples from 865 rhesus monkeys living in family groups at the Southwest and Oregon National Primate Research Centers. Based on those studies, they have been going through rhesus chromosomes and placing markers at short stretches of DNA where they have found variation from individual to individual. The idea is for researchers to be able to look at the co-inheritance of one of these markers and a specific trait they are studying. Then they know that the gene causing or influencing that trait must be located near that particular marker.

Rogers said the genetic linkage map is now developed to the point that it "can give AIDS researchers a tool they can use to find genes that influence individual variation in how rhesus monkeys respond to SIV. That could help scientists understand genetic differences in people that influence their response or susceptibility to HIV infection."



Dr. Luis Giavedoni



Baboons offer clues about epilepsy



If we want to learn more about epilepsy and spontaneous seizures — the specific cause of which is undetermined in about half of newly diagnosed cases — we might do well to look at baboons.

While a little less than 1 percent of the U.S. population suffers from epilepsy, in which seizures are recurring, and more than 5 percent of the population has had at least one seizure, scientists studying wild red baboons during the late 1960s and early 1970s found the natural occurrence of spontaneous seizures in anywhere from 40 to 100 percent of sample groups. Without contest, this makes the baboon the nonhuman primate species most susceptible to the disorder, says Dr. Jeff Williams, assistant scientist in the SFBR Department of Genetics.

“Although seizures have been observed in other nonhuman primate species, the prevalence is much lower than seen in baboons,” said Dr. Williams. “Baboons truly are a unique model organism when it comes to epilepsy.”

Although baboons’ unique susceptibility to epilepsy and spontaneous seizures has made them a focus of clinical research on epilepsy since the 1960s, no one has studied these animals to search for the genes that play a role in that susceptibility — until now.

This past fall, Dr. Williams received a \$1.15 million grant from the National Institute of Neurological Disorders and Stroke, a division of the National Institutes of Health, to develop baboons at SFBR as a natural animal model for investigations on

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the genetics of epilepsy. The intent is to find genes that influence epilepsy in baboons and then apply that knowledge to help improve the diagnosis and treatment of epilepsy in humans.

Epilepsy and seizures can be caused by anything that disturbs the brain's normal pattern of neuronal activity and can begin at any stage of life. Some cases are due to abnormal brain development, while others may have been brought on by an illness or accident that has caused brain injury or otherwise disrupted brain activity. Stress, alcohol, drugs, and sleep deprivation are among other identified possible seizure triggers. Surprisingly, the vast majority of new cases have no identified cause at all.

Genes have long been thought to play an important role because seizures can run in families. And just as people with epilepsy have different types, triggers, frequency and timing of their seizures, scientists also suspect that there are many different genes associated with this condition. Human studies already have identified several influential genes, and Williams expects that this study with baboons will help identify even more.

"We expect to validate some of the genes already identified by other researchers, and we expect to find novel, or previously unidentified, genes involved in this disorder," said Williams. "Because baboons share about 95 percent of their DNA in common with humans, it is likely that the genes we find to influence epilepsy in baboons will prove to be relevant in humans as well."

To find these genes, Williams plans to study 600 animals in the Foundation's pedigreed baboon colony. Working with the large, well-documented family groups in this colony makes it easier to follow how epilepsy runs in families and ultimately to find genes related to the disorder.

Before he begins his gene search, however, Williams is collaborating with Dr. M. Michelle Leland, veterinarian at SFBR, and Dr. C. Ákos Szabó, associate professor of medicine in the Division of Neurology at the University of Texas Health Science Center at San Antonio, to evaluate the baboon colony and diagnose the animals with epilepsy.

Part of the diagnosis relies on reports by SFBR veterinary staff, who in their daily contact with the animals have observed spontaneous seizures within the colony. "The seizures are typically benign, lasting about two or three seconds, and often subtle — they may only involve rapid blinking of the eyes, for example. This has not been a serious veterinary problem at SFBR because, except in rare cases, the seizures have not posed a real risk to the animals' health, but observations of seizures by the staff are not uncommon," Williams explained.

To diagnose the animals and determine the true prevalence of epilepsy within the colony, which Drs. Williams and Szabó are now judging to be greater than 20 percent, Dr. Szabó has been testing the animals using a method very similar to that used for testing his human patients. The baboons undergo electroencephalography (EEG), during which they are exposed to flashing lights to activate abnormal electrical activity.

"We're trying to develop a genetic model of generalized photosensitive epilepsy — defined by an abnormal electrical

Because baboons share about 95 percent of their DNA in common with humans, it is likely that the genes we find to influence epilepsy in baboons will prove to be relevant in humans as well.

— Dr. Jeff Williams

SFBR geneticist leading a new research program on epilepsy

response of the brain to the [light] stimulation," said Szabó. "This is the type of epilepsy that is frequently inherited and difficult to study in humans."

As part of the test, Szabó asks a variety of questions. Did the animal have a seizure during the EEG? If so, what kind of seizure? Did the animal have electrical discharges in the brain that are typical for human epilepsy? Did it show an abnormal response to photic stimulation? What kinds of responses were observed?

These results give Williams and his research team at SFBR specific traits they can use in their genetic research. They can then scan the genome of each animal and determine if differences in these epilepsy-related traits coincide with individual variation in the genome. "If you think of DNA as this enormous stretch of highway, we examine lots of mile markers along that highway," identified in the baboon gene map published by SFBR scientists in 2000, Williams explained. "If there is a gene near a given mile marker that is involved in one of the traits we're testing, then we get a signal near that marker. That tells me there is probably a gene somewhere in that region that is involved in epilepsy, and I know to focus in on that region to find the specific gene."

Once that gene is found, further laboratory investigations would be required to determine that gene's mechanism of action, or exactly what it is doing to influence epilepsy. "For example, does it block an enzyme, or make a different protein? What's going on at a molecular level, and how does that finally translate to the presence or absence of a seizure?" Williams asked.

Szabó said that kind of information could help him better diagnose the cause of seizures in his human patients, and in turn, he could prescribe better therapies. "Maybe this study will show us that a certain gene or genes cause a channel or receptor abnormality that contributes to the disorder," he explained. "If I could test for this abnormality in my patients, I could direct a therapy that is more specific to that epilepsy."

In the spotlight:

Trustee **Tim Hixon**



In each issue of Progress, we introduce our readers to one of the many outstanding members of our Board of Trustees. We thank Mr. George C. "Tim" Hixon for agreeing to step in the spotlight this issue. As vice president and chairman of Hixon Properties, Inc., and owner of

Hixon Land and Cattle Company, Mr. Hixon couples his business success with an extraordinary effort to improve people's lives through wildlife conservation, high-quality health care, excellence in education, and promotion of the arts. A long-time trustee who served from 1988-1998 as SFBR chairman, he has certainly made his mark on the institution that SFBR is today and will be in the future. We hope our readers enjoy this opportunity to learn about the life of a man who has been a great leader and a great friend to SFBR.



Trustee Tim Hixon in the SFBR conference room that bears his name.

You've said that, besides your wife, Karen, wildlife is your greatest love. What has made it such a passion of yours?

I'm not sure where it all started. I just remember it always being a big part of my life. I was born and raised in Jacksonville, and my grandparents had a farm in north Florida. I spent as much time there as I could, and I started fishing at a very young age. That is still something my wife and I enjoy.

Fishing and hunting trips have taken you to many parts of the world. What would describe as your favorite outdoor adventure?

That's difficult to say, but hunting with a native tracker in Zaire for bongo was certainly exciting. I do mostly fishing these days, however. My wife and I fish for trout at our ranch

in Idaho, and we recently returned from a fishing trip to Chile and Argentina. We've been to Alaska several times, and I've fished as far away as Mongolia. Saltwater fly-fishing is one of my favorite things to do. When you're poling around in a small boat in very shallow water, it's an awe-inspiring feeling to have a 100-pound tarpon going wild at the end of your line, and you're standing there with just a small fly rod in your hand.

As much as you enjoy wildlife and the outdoors, you've done a great deal of work in wildlife conservation for the welfare and enjoyment of others. A former Texas Parks and Wildlife commissioner and chairman of the Texas Parks and Wildlife Foundation, you still serve on the boards of numerous conservation groups. Your awards for your outstanding

Continued on page 18

Tim Hixon, continued
from page 17

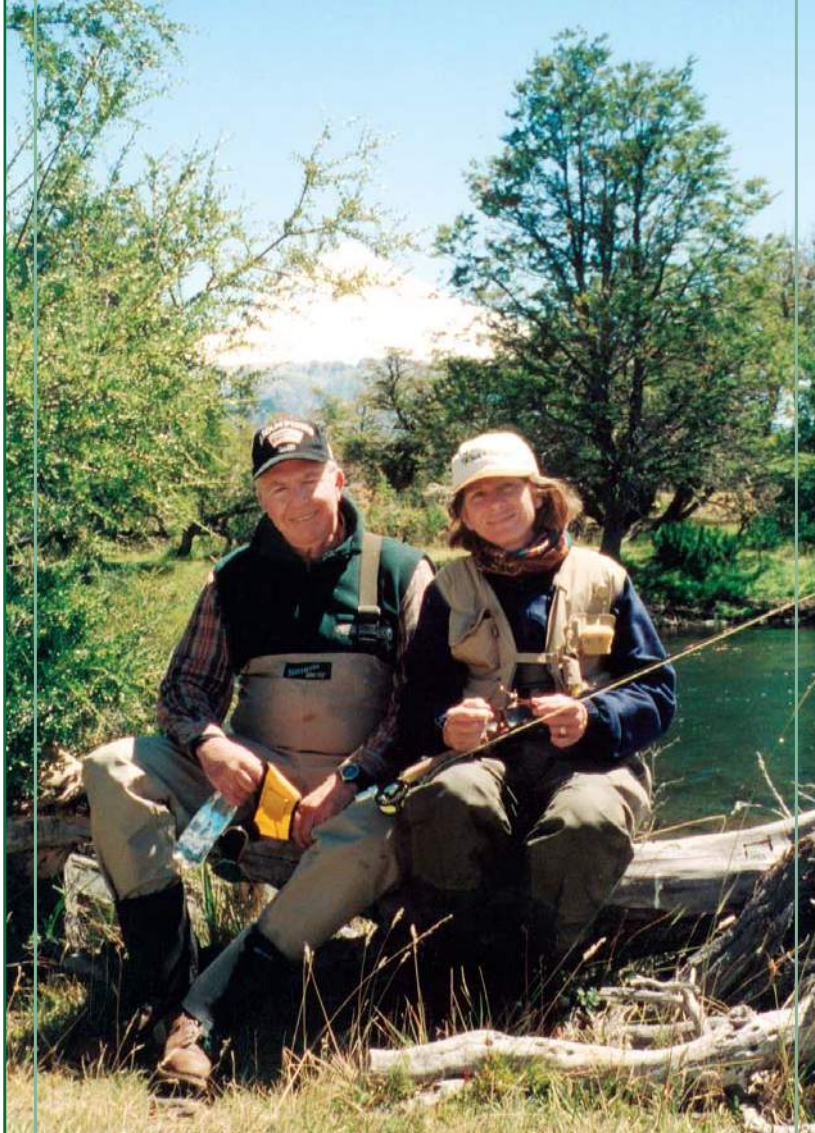
conservation efforts are also numerous, including the 2004 Texas Legends Award from the National Fish and Wildlife Foundation and Conservationist of the Year awards from Game Conservation International and the San Antonio Anglers Club, to name just a few. What do you consider your greatest accomplishment in this area, or what has been your favorite conservation project?

I think the effort I've enjoyed the most is one just west of San Antonio called Government Canyon State Natural Area. It's nearly 8,500 acres of land that sits over the Edwards Aquifer recharge zone, and while I was a Texas Parks and Wildlife commissioner, the department joined efforts to set it aside to help protect our drinking water and to provide people with some wonderful outdoor recreational opportunities.

The property is part of an old Army trail going out to various forts in West Texas, which is why it's named Government Canyon. It's a fascinating piece of land to have so close to town — just northwest of Leon Valley and west of Helotes. It's home to ancient ranch buildings, caves, and some threatened animal species, and there are dinosaur tracks in the streambed. I believe 43 miles of trails are scheduled for hiking, mountain biking and horseback riding, so the public should be able to get out and enjoy the property. It is intended to serve an educational purpose as well, which is why we built some classrooms into the visitor center. A lot of forces came together to make this happen, and now it's scheduled to open on June 4. I am happy to have been even a small part of it.

Your environmental efforts have focused on conservation, but when you served as chairman of SFBR, you initiated plans for major renovation. Seeing the aging facilities on the campus and the need to build state-of-the-art laboratories for scientists, you first spearheaded efforts to build a new SFBR campus at the Texas Research Park. When that proved infeasible, you showed flexibility and shifted the focus to rebuilding the existing campus.

Backing off plans to move the campus was one of the hardest decisions I've ever had to make, but with the crash of



Tim and Karen Hixon, who share a love for the outdoors, make fishing in Argentina an annual experience.

the real estate market in the 1980s, there was no way we could afford it. I believe we made the right decision to stay where we are.

The Campus Modernization Plan has certainly led to good things for SFBR. Your own financial contributions helped enable the first part of this plan — a new virology complex that gave scientists access to the only privately owned maximum containment laboratory in the country. You must be pleased to see the exciting research conducted in this laboratory, as well as SFBR's dramatic progress in executing the remainder of its Campus Modernization Plan.

Oh, I'm so glad about it I can't stand it. As I've told people before, the bright spot in my years of being involved with SFBR was hiring Dr. Frank Ledford as

president. He clearly took the reins on the campus modernization effort and got this important building project done. He's been remarkable, and his retirement will leave big shoes to fill.

Speaking of Dr. Ledford, I understand there is some irony in the fact that, as SFBR chairman, you hired him as SFBR president.

I was an Army medic in Korea in the early 1960s. I was Specialist 4th Class Tim Hixon, the equivalent of a corporal. Thirty years later, I had the opportunity to hire an Army three-star general who also happened to be the Army's retiring surgeon general. I had a lot of fun with that.

Were you interested in a career in medicine at one time? How did you end up as an Army medic in Korea?

We still had the draft back then, and I simply volunteered for the Army before I was drafted. In that kind of situation, you don't choose your assignment, but I enjoyed serving in Korea as a medic. We ran a fine hospital, and in my off time, I could explore the Korean countryside. But I quickly realized that the Army wasn't for me. So when I received a letter from my uncle asking me to come work for the family business, I thought that was a good idea. After my time in the Army, I came to San Antonio and finished my education at Trinity



At left and above: Tim Hixon participates in groundbreaking ceremonies for the Betty Slick and Lewis J. Moorman Jr. Laboratory Complex, for which he led the capital campaign. At right: He visits with Dr. Andrew Hayhurst to learn about his research on SARS, one of various agents under investigation in that laboratory complex.



University. Then I went to work for Midland Investment Company, the predecessor to what is Hixon Properties today.

Was it your uncle, Fred C. “Colonel” Hixon, who got you involved with SFBR? He was a trustee for more than 20 years and a major supporter. In fact, you and he together donated the funds for SFBR to build its Hixon Research Hospital.

My uncle was a good friend of [SFBR founder] Tom Slick and a strong supporter of the Foundation. In fact, I believe [under his leadership] Midland Investment Company loaned the Foundation money back in the 1950s to help make salaries. He certainly had a big influence on me, but I can’t remember just exactly how my affiliation with the Foundation started. I just have always been interested in the type of work it does, appreciating that its scientists are dedicated to curing horrible diseases.

While I can’t recall who said it, someone likened biomedical research to a pyramid of sand. Each bit of research adds one grain of sand to the pyramid. Finally, the one who gets all the glory is the one who drops that last grain of sand on the pyramid. Hopefully the Foundation will be that organization at some point, but we’ve certainly contributed millions of grains of sand to that pyramid.

Did you enjoy serving as SFBR chairman?

I loved it. I was fascinated by the whole process — the process of research, of how a research organization functions, and how it is funded. It can be a little scary sometimes thinking how much of the budget comes from the National Institutes of Health. What if NIH has to cut its budget? Government can give, and government can take away. That is why I believe it is so important for the Foundation to build up its endowment, but those are hard dollars to raise.

While you’ve done much to advance biomedical research and wildlife conservation, you and your wife also are big supporters of the arts and education in San Antonio. Besides serving as a trustee for Trinity University and the McNay Art Museum, for example, you and your wife were major contributors to the preservation and

restoration of the Majestic Theatre and the Charline McCombs Empire Theatre, as well as the development of the San Antonio Performing Arts Center. Is your guiding philosophy to help build a well-rounded community environment that meets people’s diverse needs?

My wife really is much more involved with the arts than I, but yes, I’m a believer in support of the whole. The reason I’ve been a supporter of the San Antonio Symphony for 40 years is that I believe in a well-rounded community. I think that is very important, and I know when the city is trying to attract major businesses to come here, that is one of the top-of-the-list factors they consider.

Biotechnology is another important part of that whole, and Southwest Foundation is a main contributor to this vital industry in San Antonio. It is a big plus for the community. The Foundation has come so far since Harold Vagtborg’s days [as its first president]. I’m sure Harold is looking down thinking, “Good job,” and I would suspect Tom Slick is, too.



Tim Hixon’s appreciation for nature and art come together in the offices of Hixon Properties.



One of the most elemental drives that powers humans is to have an impact, an impact that is both strong and sustaining. When we raise children, we impact the future. When we influence a friend or loved one, we impact the future of humankind.

The coming together of many individuals who desire to impact the future is one of the strongest forces in our civilization and is often referred to as philanthropy — altruistic concern for humankind. Philanthropy has created great institutions such as the Southwest Foundation for Biomedical Research. Beginning with our founding more than six decades ago and extending to the enabling endowment and donations we invest in life-saving research, it is philanthropy that sustains the institution today.

Philanthropy and SFBR are natural partners. The reason is simple: If you desired to impact the future of human health, it would be difficult to achieve such an ambitious goal all by yourself. However, there is power in joining with other like-minded individuals who share your dream for a healthier tomorrow.

Imagine ... if you could discover the cure for a devastating health condition like cancer, cardiovascular disease or diabetes.

Imagine ... if you could create the vaccine that would obliterate a killer virus.

Imagine ... if you could identify the genes that cause one of civilization's most debilitating diseases.

It is this kind of imagination that has led to many amazing medical developments that are saving lives today — advances that scientists only dared to dream about a few decades ago. You can be a part of efforts to develop the life-saving advances for the future — a future that today we can only imagine.

Join today ... become a Golden Circle member

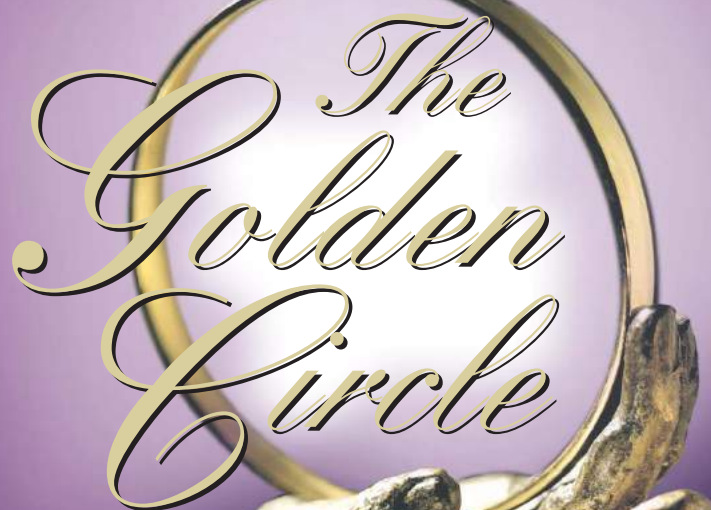
The Golden Circle was established in 1977 to further the ability of SFBR to reach its goals and attain international status in the field of biomedical research. This commitment has a direct impact on the health of people worldwide through new and innovative research.

Golden Circle contributions often provide “seed money” that facilitates the early pilot studies necessary to garner major grant funding from sources such as the National Institutes of Health. Donations also support the acquisition of laboratory equipment as well as the recruitment of new scientific faculty.

By becoming a member of the Golden Circle, you can join in the valuable efforts of an organization that shares your dream.

Membership opportunities

Individuals, companies and foundations may become members of the Golden Circle by making an annual contribution at one of the following levels:



*Doing more together
than we can do alone*

- **Golden Circle**, unrestricted contributions of \$1,000 or more for the direct support of indispensable biomedical research.
- **Benefactor Circle**, unrestricted contributions of \$2,500 or more that also fund vital biomedical research.
- **President's Circle**, contributions of \$5,000 or more to support SFBR's growing need for state-of-the-art laboratory equipment.
- **Chairman's Circle**, contributions of \$10,000 or more to fund strategic initiatives that require immediate investment at the discretion of the chairman and Board of Trustees.

Heartfelt rewards

Your generosity contributes to the advancement of biomedical research at SFBR. When you become a member of the Golden Circle, you help provide a healthier tomorrow for all humankind.

As a member you will receive a prestigious award designed by New York artist Alex Ettl. This personalized award serves as a constant reminder of your goodwill.

Additional benefits include the opportunity to attend an annual dinner at The Argyle, exclusive events, briefings, receptions and VIP tours, along with travel and cruise invitations. As a member, your name will be listed according to your membership level in the annual *SFBR Report of Progress*.

Furthermore, your contribution assists in augmenting the ability of SFBR to garner federal grants. For every dollar you give, SFBR has historically raised another \$8, for an 800 percent return on investment, thus fostering even more research to find cures for life-threatening diseases.

We invite you to open your heart and become a part of the Golden Circle, through which humanitarianism and biomedical research work together to build a brighter future for people living today and for generations to come.

Golden Circle reception an evening of gratitude

Each year, to thank Golden Circle members for their important contributions to biomedical research, SFBR hosts two special events in their honor: an appreciation dinner in the spring featuring a scientific update from an SFBR faculty member, and an evening reception in the fall that simply allows members to reconnect with the Foundation and one another.

This past December, the tables were turned slightly, as the honorees gathered at The Argyle to express their gratitude to SFBR President Frank F. Ledford Jr., M.D., along with his wife, Marilyn, for 13 years of dedicated service to the Foundation. It was an enjoyable evening for all and a fitting way to honor Dr. Ledford before his retirement.

Shown here are just a few of the evening's special guests:



*Yes, I would like to join
the Golden Circle today!*

Individuals, companies and foundations may become members of the Golden Circle by making an annual contribution at one of the following levels.

Please check the appropriate box:

- ☐ **Golden Circle**, unrestricted contributions of \$1,000 or more to directly support indispensable biomedical research.
- ☐ **Benefactor Circle**, unrestricted contributions of \$2,500 or more which also fund vital biomedical research.
- ☐ **President's Circle**, contributions of \$5,000 or more to directly support the growing need for state-of-the-art equipment.
- ☐ **Chairman's Circle**, contributions of \$10,000 or more to fund strategic initiatives that require immediate investment at the discretion of the Chairman and Board of Trustees.

To join the Golden Circle online, go to www.sfbr.org and click on "Find out more" in the Golden Circle section.

Dr./Mr./Mrs./Ms.

Name

Spouse's Name

Home Address ☐ Check if preferred mailing address

City

State

Zip

Home Phone

Business Phone

E-mail

Business Title

Company or Foundation Name

Business Address ☐ Check if preferred mailing address

City

State

Zip

Payment options:

To pay with credit card (please check card type):

☐ MasterCard ☐ Visa ☐ American Express ☐ Discover

Card #

Exp. Date

Name on Card

Billing Address

City

State

Zip

To pay by check (please complete the following information):

My annual membership in the amount of \$_____ is enclosed.

Please make your check payable to SFBR. **Your contribution is tax deductible.**



Southwest Foundation Forum

Planting seeds for a brighther future

Spring is in the air, and the contagious enthusiasm of the Southwest Foundation Forum is in full bloom. This peak time of the Forum year includes a full line-up of fun-filled events to support SFBR and its mission of biomedical research.

Between January 19 and March 30, the Forum hosted 10 separate SFBR tours for upper-level science students from regional high schools. These tours provide wonderful opportunities for students to see how their classroom studies can be applied to life-saving research efforts, hopefully inspiring some of these bright young students to pursue research careers themselves. In addition to a tour of campus facilities, students get the opportunity to learn about SFBR's history and the inspirational story of its founder, Tom Slick, and they meet with an SFBR scientist whose work helps fulfill Mr. Slick's dream of improving human health through scientific research.

On Wednesday, March 23, local high schools benefited once again from the Forum's efforts. Members attending the light-hearted spring lecture luncheon enjoyed hearing local psychologist Dr. Madeleine Reichert speak on the topic "Can We Be Saintly and Still Be Sane?" Some of the most enthusiastic attendees, however, were science teachers who received grant awards for an innovative science program at their schools. Thanks to the generous support of the V.H. McNutt Memorial Foundation and the L.D. Ormsby Foundation, the Forum was able to present five awards totaling \$14,000 to the following schools: Samuel Clemens High School for its first- and second-place winning entries; Alamo Heights High School, third place; and Texas Military Institute and Brackenridge High School, tied for fourth place. Congratulations to all the winners, whose applications rose to the top when judged by a panel that included Forum board members, V.H. McNutt Memorial Foundation members, and SFBR scientists.

Also in March, Forum members and other invited guests from the Golden Circle and Founder's Council gathered at SFBR for the Forum Evening Tour. Following a lovely reception in the Corwin D. Denney Conference Center, guests walked the campus grounds to see the Foundation's acclaimed baboon colony and to visit the offices and laboratories of SFBR scientists. There they heard from some of the Foundation's leading investigators about the latest progress in their research projects on cancer, infectious diseases, and the influence of genetics on a wide variety of diseases.

Now Forum members are gearing up for their premier event, the annual spring gala. An outstanding fundraiser that provides grants for innovative pilot studies by SFBR scientists, the gala also is one of San Antonio's most anticipated social events. This year's event — scheduled for Saturday, May 14, at The Argyle — is the group's 35th gala, and it promises to impress. Describing how the theme "A Medieval Knight: An Evening to Remember" will be carried out, Gala Chair Karen Heydenreich said, "We will have medieval ambiance unmatched before in San Antonio, including living, breathing knights to greet you as you arrive, as well as a feast fit for a king, magical music and phenomenal prizes."

If you would like to participate in this fabulous event, contact Gala Co-Chair Phyllis Viola at 210-930-7100. Tickets are on sale for \$175 each. The ladies of the Forum also continue to recruit volunteers, as extra hands are helpful even the day of the event.



Above: Forum members and guests enjoy an evening reception and tour of SFBR. Below: Churchill High School students learn about SFBR research as part of a Forum-sponsored student tours program.



The Founder's Council

Celebration enables scientific progress

The important work of several SFBR scientists is running a little more smoothly these days thanks to contributions from the Founder's Council. At the group's annual holiday party, held Dec. 8 at the Tobin Estate, the Council awarded eight grants to seven SFBR investigators to help with their equipment needs.

The two leading grants were given in honor of the late Albert Steves IV, a beloved Founder's Council friend and SFBR employee for many years. One of these grants was awarded to Dr. John VandeBerg for the purchase of a gel imaging system that will be used by several SFBR geneticists in their research on a broad range of diseases. The other went to Dr. Christina Grassi for a Yamaha Pro Hauler. This handy vehicle is making a big difference in the daily work of animal enrichment staff, who frequently need to transport toys, treats, and equipment to the various animal housing facilities on the SFBR campus.

Other Founder's Council grants were awarded to the following recipients:

- **Dr. Ricardo Carrión Jr.**, for a digital camera to document data from his studies of hemorrhagic diseases and bacterial threats
- **Dr. Lorena Havill**, for a freezer to store bone samples used in her studies on osteoporosis
- **Dr. Laura Cox**, for special equipment that freeze-dries samples used for studies on atherosclerosis, hypertension and maternal nutrition
- **Dr. John VandeBerg**, for a microscope to monitor and manage live cultures used in his research on Chagas' disease, a parasitic infection that can cause heart failure and digestive disorders
- **Dr. Zhiqiang Wang**, for various instruments used in his research on the repair of spinal cord injury and the treatment of cancer
- **Dr. Andrew Hayhurst**, for a pair of large-volume pipettors, a multi-unit dispenser that will increase the speed of isolating antibodies for his research on hemorrhagic fevers and SARS

These grants, which totaled nearly \$25,000, would not have been possible without the dues contributions of Founder's Council members, other generous gifts to the Albert Steves IV Memorial Fund, and an extraordinary contribution from Dr. Frank Ledford's President's Fund. Thanks to all who made this year's grant awards the best in Founder's Council history.

The Council also extends a heartfelt appreciation to the generous sponsors of the group's holiday party: The Tobin Foundation; Loeffler Tuggey Pauerstein Rosenthal LLP; and



SFBR scientists who received Founder's Council grants (above) and Founder's Council members enjoy the group's holiday party at the Tobin Estate.



The BMW Center. Their event sponsorship allowed the Council to direct more of its dues income toward grants to SFBR scientists.

This spring, the Founder's Council has been busy with events that inform members and the San Antonio community about the life-saving and life-improving research of SFBR, including a speaker luncheon featuring Dr. John VandeBerg on Feb. 23 and the Forum Evening Tour of SFBR on March 9. Numerous other receptions and luncheons are scheduled for the remainder of the year.

If you would like to join this group and support its worthwhile efforts, contact Amy Abdalla at 210-258-9409 or amy@sfbr.org, or log onto http://www.sfbr.org/pages/founder_council.php.

About Southwest Foundation

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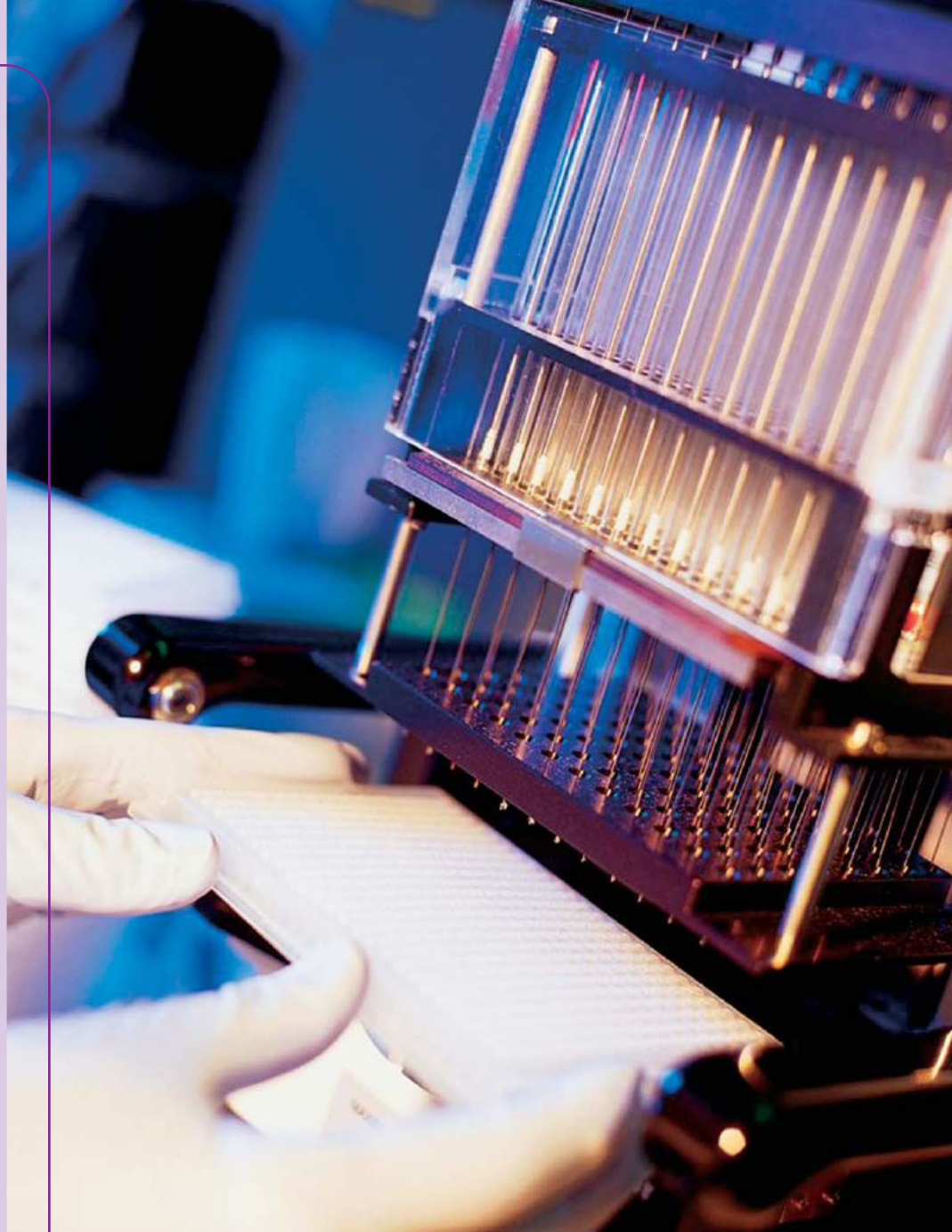
As one of the world's leading independent biomedical research institutions, the Southwest Foundation for Biomedical Research is advancing human health. Today, SFBR's multidisciplinary team of nearly 75 doctoral-level scientists work together on more than 175 major research projects.

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 Web site, www.sfbr.org.



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