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PROGRESS

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SAN ANTONIO FAMILY ASSESSMENT
SAFARI
OF METABOLIC RISK INDICATORS

Improving children's health

INSIDE:

Message from the President

John C. Kerr

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Every time I step onto the Foundation campus, I seem to discover a new reason to renew my commitment to this stellar research institution and its focus on improving human health through innovative biomedical research. I understand why our founder, Tom Slick, enjoyed being an active leader who went into laboratories or sat at roundtables with scientists to engage in conversation about their research projects – it's exhilarating to see powerful, creative minds at work trying to tackle the pressing health problems of our time.

One example is Dr. Harald Göring. One of our rising stars in the Department of Genetics, he recently received a major new grant award from the National Institutes of Health to look at one of our country's top killers, cardiovascular disease, in an entirely new way. He is studying genetic factors influencing our susceptibility to common chronic infections – including the virus that causes cold sores – and how that might increase our risk for cardiovascular disease by creating a constant state of inflammation in our bodies.

Dr. Ravindranath Duggirala's genetic studies are aimed at tackling diabetes as well as cardiovascular disease, but he is trying to get to the root of the problem through a collaborative study examining metabolic syndrome, a precursor to both diseases, in children. As you will see in this issue of our magazine, the young people involved in this project are on an exciting SAFARI to improve their own health and the health of generations to come.

Meanwhile, Drs. Peter Nathanielsz, Laura Cox and a team of other scientists from SFBR and the University of Texas Health Science Center at San Antonio are uncovering new data showing the importance of adequate nutrition for expectant mothers wanting to give their babies a healthy start at life.

Also in this issue, you'll learn more about Dr. Rebeca Rico-Hesse, whose previous work with the Centers for Disease Control and Prevention led to new epidemiologic methods that influenced the World Health Organization's efforts to eradicate polio. Today, she is busy at SFBR trying to tackle the emerging threat of the dengue virus, which reached South Texas in its most dangerous form in 2005. That same year, she developed the first animal model for studying this mosquito-borne virus, setting the stage for studies at SFBR and around the world to test the efficacy of potential vaccines and antiviral therapies.

> **…it's exhilarating to see powerful, creative minds at work trying to tackle the pressing health problems of our time.**

It is my hope that these stories will give you a sense of the remarkable breadth of research I see at SFBR on a daily basis. These cutting-edge research projects represent the fulfillment of Tom Slick's dream of creating a great center for human progress through research, as you will see in our trustee spotlight with Leroy Denman. A founding trustee of SFBR, Mr. Denman drafted the trust instrument Tom Slick used to make his dream a reality. Ever since, he has devoted his time to furthering the dreams not only of Tom Slick but of many other prominent South Texas families and businesses. I thank him for sharing his stories and insights with our readers in this issue.

I also thank you, the Foundation's friends and supporters, for your continued generosity to this organization. Like Tom Slick and Leroy Denman, you are enabling visionary scientific efforts to saves lives and improve human health.

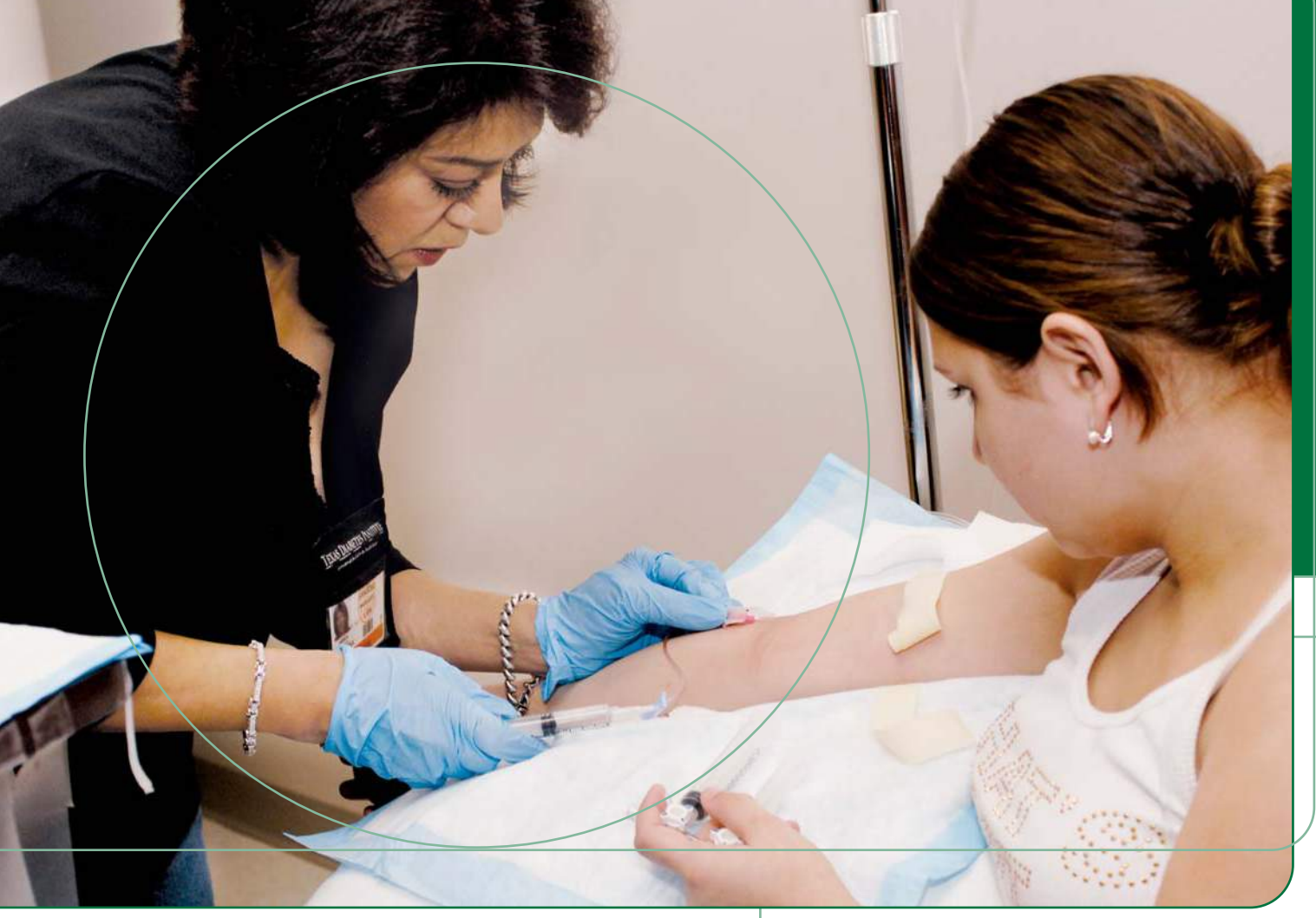
On SAFARI to improve children's health

A DEXA scan to measure body fat is part of the adventure for SAFARI participants.

Some local children might feel a little bit like Dora the Explorer, volunteering to go on SAFARI with San Antonio doctors. But instead of a trip to Africa to encounter exotic wildlife, these youngsters – 750 of them, ages 6 to 17 – are heading to the Texas Diabetes Institute (TDI) on Zarzamora Street in San Antonio.

There they undergo a series of physical tests that include a body fat scan, a measure of their resting energy expenditure, an examination of their brachial arteries, a glucose tolerance test, and a wide variety of other health assessments. They're even doing a step-test to assess their cardiovascular fitness and wearing accelerometers that allow doctors to get precise measures of their daily physical activity. All the results, along with blood samples for genetic testing, are sent to scientists at Southwest Foundation for Biomedical Research (SFBR).

What kind of SAFARI is this, you might ask? It's the **S**an **A**ntonio **F**amily **A**ssessment of Metabolic **R**isk **I**ndicators in Youth study, recently funded by the National Institute of Child Health and Human Development with a new five-year, $2.3 million grant. ▶ *Continued on page 4*



A SAFARI participant gives a blood sample for a glucose tolerance test.

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Headed by principal investigator Dr. Ravindranath Duggirala, a genetic epidemiologist at SFBR, it is a collaborative effort by researchers at SFBR, the University of Texas Health Science Center at San Antonio, the University Center for Community Health/TDI, and the UT Health Science Center – Houston School of Public Health, San Antonio Program.

Dr. Daniel Hale, chief of the Division of Pediatric Endocrinology and Diabetes in the Department of Pediatrics at UTHSCSA, serves as medical director for the SAFARI study. Along with Dr. Hale, other physicians who examine study participants include Drs. William Rogers, Rolando Lozano and Jane Lynch.

Researchers in the program are indeed on an adventurous expedition, but it's an expedition to learn more about how some traditionally adult diseases are impacting our children, and ultimately, to find new ways to prevent and treat those conditions.

The particular focus for this study is how genetics and the environment work together to determine a child's susceptibility to metabolic syndrome and type 2 diabetes – health problems formerly associated with adults but that have become all too prevalent in our nation's youth in recent years.

What is metabolic syndrome?

Metabolic syndrome refers to a cluster of disease risk factors that include obesity, high blood pressure, low HDL cholesterol (the "good" cholesterol), high triglyceride levels, and high glucose values or insulin resistance. Metabolic syndrome increases a person's risk for developing type 2 diabetes, as well as cardiovascular disease.

"If you have three or more of these five risk factors, you are considered to have metabolic syndrome," explained Dr. Duggirala. "This condition affects more than 47 million Americans, and Mexican Americans are particularly susceptible. They have the highest prevalence of metabolic syndrome of any ethnic group, with 32 percent of Mexican American adults affected."

But he cautions that the concern is not just with adults. "Within the last two decades, we've seen an increase in metabolic syndrome and type 2 diabetes in children. Some overweight children as young as 4 years old are already afflicted with metabolic syndrome," Dr. Duggirala said.

The interplay of genes and the environment

Why is this happening, and what can we do to curb this mounting problem? Dr. Duggirala and his collaborators believe the answers lie in the story of our genes, our environment and lifestyle, and how they all interact.

"Certainly genes play a role in our susceptibility to disease, but our genes haven't changed much in recent years," said Dr. Duggirala. "However, the food we eat and our level of physical activity have changed, and we know that genes and the environment act on each other. So do the individual differences in susceptibility to metabolic syndrome relate to the way our genes are responding to these changing environmental factors? One of the aims of our study is to find the answer to that question. We want to find the genes that increase our susceptibility to metabolic disorders, and we want to see how those genetic influences are altered by the environment."

Investigators also want to know if the same genes are at play in both children and adults. "It may very well be that the same genes are involved in both cases, but we might also find that different sets of genes are involved at different ages," explained Dr. Duggirala.

SAFARI Medical Director Dr. Daniel Hale, Study Coordinator Sharon Fowler, and Principal Investigator Dr. Ravi Duggirala meet with Research Associate Roy Resendez to discuss brachial artery sonogram results for one SAFARI participant.

Finally, the most basic order of business of the study is to learn more about metabolic syndrome in children. "Metabolic syndrome has been well documented in adults, but it has not been studied much or adequately defined in children," Dr. Duggirala said. "We want to document its prevalence in Mexican American children, and we want to see if the profile of metabolic syndrome is the same for children as it is for adults."

Building on previous progress

You might imagine that the answers to all these questions lie in more than just one study – and you're right. Participants in the SAFARI study all are children of adults who have been participating in one of three long-term studies sponsored by SAFARI collaborators. All three were started in the early 1990s, and all are large-scale, multi-generational family studies focused on the genetics of metabolic disorders in adult Mexican Americans living in San Antonio. They include the San Antonio Family Heart Study, the San Antonio Family Diabetes/Gallbladder Study, and the Veterans Administration Genetic Epidemiology Study.

Results from these various studies will be compared with SAFARI findings to see, among other things, if the metabolic profiles of children match their parents, if the definition of metabolic syndrome is the same in both groups, and what genetic factors are influencing variation in metabolic syndrome in the children and in their parents.

"Through these and other studies, scientists have identified a number of candidate genes that appear to play a role in the development of metabolic syndrome," said Dr. Duggirala. "As part of the SAFARI study, we're going to look at the influence of 25 of those genes in children to see if they have the same influence on metabolic syndrome that they appear to have in adults."

Benefits for children and their families

The ultimate goal of all this is to find better ways to prevent and treat disease. "If we can identify a particular genetic marker or a particular biochemical profile that shows there is a subset of children who are at particular risk for diabetes or cardiovascular disease, then very specific intervention programs can be designed to prevent disease in those individuals," said Dr. Hale.

"For parents and primary care physicians, it's also a good motivating factor to intervene early if you discover that your child is at greater-than-average risk of developing diabetes or cardiovascular disease at an early age," Dr. Hale continued. "And the earlier we intervene, the better. The treatments for metabolic syndrome are much simpler if you initiate them when an individual only has elevated lipids, for example, as opposed to waiting until the person has a heart attack or stroke."

That is why researchers are doing what they can to help parents of study participants intervene now. Eventually, they would like to add an intervention component to the SAFARI study, where researchers design and oversee tailored intervention programs for participants found to have metabolic syndrome or even diabetes. But that will require additional grant funding.

For now, they are alerting parents whose children are found to be at risk, making recommendations on beneficial lifestyle changes, and offering information on where parents can go to seek medical care. In some cases, parents might even be notified that their children are eligible to participate in a different, intervention-focused study sponsored by TDI, UTHSCSA, or one of the other collaborating institutions. "That's part of the beauty of us all working together on this project," said Dr. Hale.

Sharon Fowler, a UT Health Science Center faculty associate who serves as the study coordinator for SAFARI, emphasized the importance of giving feedback to parents. "Certainly we want to help future generations, but we also want to help families now," she said. "By giving these parents feedback on their children's disease risk factors, we give them important knowledge, and knowledge is power."

Could an infection break your heart?

New genetic study examines link between infections, cardiovascular disease

A new grant to Southwest Foundation for Biomedical Research (SFBR) will allow scientists to look for genetic factors that increase our susceptibility to some of this country's most common chronic infections, and ultimately, how that susceptibility might be linked to our risk for cardiovascular disease.

Dr. Harald Göring, principal investigator of the new $1.9 million grant from the National Heart, Lung and Blood Institute, titled "Genetics of Infection and Its Relation to CVD Risk," says there has not been extensive research on the role infections play in the risk for cardiovascular disease. However, a number of epidemiological studies have shown a higher-than-average prevalence of infections among people who have suffered heart attacks, strokes, and a variety of other ailments.

He says a leading hypothesis explaining this correlation is that chronic infections lead to a chronic state of inflammation, as the immune system works continuously to fight off the infection. "In recent years, it has become

Dr. Harald Göring is taking a new approach in the battle against cardiovascular disease, looking at how one major risk factor for heart attacks and strokes might be tied to our genetic susceptibility to chronic infections. The AT&T Genomics Computing Center at SFBR will play a large role in his search for disease-influencing genes.

apparent that inflammation is a central feature of some chronic diseases of old age, and it's particularly well established as a risk factor for atherosclerosis (hardening of the arteries) and cardiovascular disease," Dr. Göring said.

"So the obvious question becomes, 'What gives rise to inflammation?'" he continued. "Inflammation typically has some underlying cause, something that leads the immune system to respond to something. It's not unreasonable to think that a chronic infection with some type of virus or bacterium – even if that infection is not causing acute symptoms – would keep the immune system continually at work and lead to some overall systemic inflammation, as well as inflammation at a specific site [in the body] where the pathogen might be hiding."

Therefore, he says, if we could find better ways to control infections, we might reduce risk for cardiovascular disease and other conditions affected by inflammation in the process.

Ongoing local studies could help answer new questions

To study this whole issue, Dr. Göring is collaborating with Drs. Charles Leach and Ellen Kraig at the University of Texas Health Science Center at San Antonio in a close look at participants from three major San Antonio studies: the San Antonio Family Heart Study, the San Antonio Family Diabetes/Gallbladder Study, and the Veterans Administration Genetic Epidemiology Study.

All three studies involve large, multi-generational family groups from the San Antonio area; all are focused on the genetics of metabolic diseases, where inflammation plays a major role; all involve Mexican Americans, so participants are from the same ethnic background; and all have genetic samples and various health measures readily available for examination in this new study.

Using data from 2,500 participants of these three studies, Dr. Göring's first goal is to determine how many of these individuals test antibody-positive for current or previous infection with one or more of seven selected pathogens, and then to search for genes that influence their susceptibility to infection with these pathogens.

Why these seven pathogens?

"For this study, we specifically selected seven infectious agents that have shown some correlation with cardiovascular disease, that are capable of eliciting chronic infections, that are transmitted through the respiratory tract, and that are so common in the environment that we can presume just about everyone has been exposed to them multiple times," said Dr. Göring.

These pathogens include *Chlamydia pneumonia*, a common cause of pneumonia; *Helicobacter pylori*, a major cause of ulcers; *Porphyromonas gingivalis*, commonly associated with gum disease; hepatitis A virus, most commonly spread among school-age children and young adults; herpes simplex virus 1, the cause of cold sores; *Cytomegalovirus*, or human herpesvirus 5, which particularly affects the salivary glands; and human herpesvirus 8, which induces Kaposi sarcoma in persons with immunodeficiency.

"What we want to know is, since these pathogens are so common and so easily spread, how have some people managed to avoid infection?" asked Dr. Göring. "Everyone has been exposed to them, but some people don't have antibodies for them in their bloodstream, indicating that they've never been infected with these pathogens and mounted an immune response. So they may have some innate resistance to infection, some other way of preventing infection in the first place. That could be due to a difference in their genetic makeup."

In a pilot study with 600 individuals from the San Antonio Family Heart Study, Dr. Göring has already shown evidence that there are genetic variants on chromosome 21 that influence susceptibility to *Chlamydia pneumonia*. Now he wants to look for genetic influences on susceptibility to all seven pathogens in a larger study population.

In addition, he plans to examine the study population to see if there is a correlation between infection with these pathogens and markers for inflammation, such as high levels of C-reactive protein. That could help validate the hypothesized link between infection and cardiovascular disease, and it could allow Dr. Göring to search for genes that influence both.

Potential payoff

He believes the study could have multiple payoffs for human health. "The more we know about the relationship of infection and inflammation, the more likely people are to try to decrease infection levels," he said. "And certainly, it's feasible to treat many bacterial infections with antibiotics. But if we can find genetic factors that influence susceptibility to infections, it might also provide new ideas for how to design effective vaccines."

Besides that, "There are so many things that we still don't know about our immune system and how it works," he said. "Potentially, the identification of genetic factors involved in fighting infections might tell us something new about the function of the immune system and give us new ideas for fighting disease."

Eating for two

New evidence of how mom's diet impacts baby's future health

In a study investigating developmental programming, or how the development of the fetus in the womb affects that individual's lifetime health, researchers have found new evidence emphasizing the critical need for expectant mothers to get adequate nutrition. The study shows that even moderate maternal nutrient restriction can impair kidney development in the fetus, a problem that has been associated with hypertension in adulthood.

The collaborative project between scientists at the Center for Pregnancy and Newborn Research at the University of Texas Health Science Center at San Antonio and Southwest Foundation for Biomedical Research (SFBR) and its Southwest National Primate Research Center showed that when pregnant baboons received only 70 percent of their normal caloric intake – roughly the equivalent of someone going on a slimming diet – their fetuses experienced stunted renal growth. Their kidneys' filtering units, called tubules, were shorter and straighter than those of fetuses whose mothers were allowed to eat as much as they wanted during pregnancy.

"This is very important, because the kidneys are the body's clearinghouse," said Dr. Peter Nathanielsz, director of the Pregnancy and Newborn Research Center at the UT Health Science Center and an adjunct scientist at SFBR. "The kidneys are constantly filtering impurities from the blood. But with shorter tubules, this filtering process is also shortened, and the kidneys aren't able to do their job adequately."

Dr. Nathanielsz explained that this can lead to high blood pressure as part of the body's natural defense. When the body detects that its blood is not being properly filtered, it raises its blood pressure to pump more blood through the kidneys and boost the filtering process. "But if your kidneys are already damaged, they're not going to be able to succeed [in adequately filtering the blood]. Over time, this increased stress on the kidneys will damage them even further," Dr. Nathanielsz said.

That is why, in a paper published earlier this year in the *Journal of Physiology*, the research team concluded, "The negative impact of poor maternal nutrition on the fetal kidney … may have important implications for postnatal renal function, thereby contributing to the observed increased predisposition to hypertension and renal disease in the offspring of nutrient restricted mothers."

The reason for the effect – how genes are at play

In addition to finding evidence of restricted renal development in the fetuses of moderately undernourished baboon mothers – the first evidence of its kind in a nonhuman primate, verifying findings from other studies with rats and

guinea pigs – the research team also uncovered the mechanism by which this occurs.

As the first group ever to apply the use of powerful gene arrays called "gene chips" to a study on developmental programming in primates, scientists looked at the expression of genes across the entire genome of baboons in the study. What they found was that the cells in the kidneys of the fetuses whose mothers were moderately undernourished during pregnancy were expressing, or using, different sets of genes than the fetuses whose mothers consumed their full diet.

"Different sets of genes were active and different sets were inactive in the two groups of baboons whose mothers ate all they wanted and those whose mothers were nutrient deficient, and we found these genetic differences to be consistent with the structural changes seen in the fetal kidneys," said Dr. Laura Cox of SFBR, the molecular geneticist on the study and lead author on the team's publication in the *Journal of Physiology*. "This helps us understand the physiological mechanism behind the stunted renal growth in the nutrient-restricted group."

Implications in the United States

Dr. Cox says that besides being a first of their kind, the study results are somewhat surprising considering the moderate nature of the maternal nutrient restriction. "Since we only restricted caloric intake by 30 percent, many people [in the scientific community] didn't think we would see much impact on the developing fetus," she said.

Explaining why the group chose this moderate level of nutrient restriction, Dr. Nathanielsz said, "We wanted to see the impact of a diet that might be experienced by women in the Western world. It's realistic that women in the lower socio-economic area of society might consume 30 percent fewer calories than recommended. This also might be the case with women of any economic status who diet during pregnancy to avoid gaining unwanted pounds."

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Drs. Peter Nathanielsz and Natalia Schlabritz-Loutsevitch look at the impact of maternal nutrition on the development of fetal kidney tubules.

> **The overarching question is, does maternal nutrition impact the longterm health of the offspring?** – Dr. Laura Cox

Dr. Laura Cox (left) and Terry Vetters (top right) run DNA analyses in the laboratory to see how maternal nutrition affects genetic expression, or activity, in the developing fetus.

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The larger questions about lifetime health

Dr. Cox explained that this particular study on the effect of maternal nutrition on the fetal kidney, funded by the National Institute of Child Health and Human Development, is really part of a much larger investigation.

"The overarching question is, 'Does maternal nutrition impact the health of the offspring? By restricting the diet of the mother, are you setting an individual up for a higher risk of atherosclerosis, diabetes, hypertension and obesity?'" she asked. "By looking at the kidney in particular, we're focusing more specifically at the issue of hypertension, but it's still part of the bigger question about post-natal health."

The same study also is looking at the impact of maternal nutrition on other areas of fetal development, such as the structural development of the liver.

Thanks to a new grant from the National Center for Research Resources, the research team also is examining how moderate maternal nutrient restriction affects baboons' lifetime health – and ultimately, people's health – by following infant baboons through their first four years of life. Among other things, they are looking to see if the impaired kidney development in the nutrient-restricted group does in fact increase susceptibility to renal disease and hypertension.

"Other studies have shown this to be true in rats and guinea pigs, so now we want to look at the similarities and differences in the long-term impact on baboon health," said Dr. Nathanielsz. "It's important to do this investigation in animals most similar to humans in genetics and physiology if we want to know more about the implications for human health, and the Southwest National Primate Research Center at SFBR is the best place in the world to do this research."

In addition to Drs. Nathanielsz and Cox, other researchers involved in these studies include Drs. Robert Shade and Gene Hubbard of SFBR; Drs. Mark Nijland and Jeffrey Gilbert of the Center for Pregnancy and Newborn Research at the UT Health Science Center; and Drs. Tom McDonald and Natalia Schlabritz-Loutsevitch, who serve at both institutions.

The "I" in science:

Dr. Rebeca Rico-Hesse

Advancing her lifelong goal to defeat emerging viruses

From an early age you knew you wanted to become a virologist who studied Venezuelan equine encephalitis. How did you develop such a specific interest?

I was interested in biology ever since I can remember, probably from seeing my father go through his post-graduate medical training. My mother told me that when I was 6 years old I declared my intention to get a doctoral degree from an Ivy League school.

My high school biology teacher sparked my interest in viruses. He told us that viruses are the smallest organisms known, simply genetic material surrounded by a coat of protein, yet they've changed the history of humanity. That made a huge impression. Then I saw the impact of viruses firsthand. In Saltillo, Mexico, where I grew up, citizens commonly shot rabid dogs in the street. And my father, as the only orthopedic surgeon in town, specialized in surgery reconstructing the paralyzed legs of patients with polio.

My interest in Venezuelan equine encephalitis (VEE) developed in the early 1970s when an outbreak swept through Central America, Mexico and into South Texas. I remember looking at the *Laredo Times*, the American newspaper to which we subscribed. The cover showed a photograph of horse carcasses being put into pits with bulldozers.

There was a tremendous effort to stop the spread of the epidemic, and the American military got involved. They tried to establish vaccine barriers and at one point set up a vaccination post outside of Saltillo. People from different areas herded their equines together, and we took them 10 miles to the vaccination post.

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Dr. Rebeca Rico-Hesse has her focus set on viruses threatening to take hold in the United States.

Dr. Rebeca Rico-Hesse puts research samples in a "deep freeze."

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It was amazing. Impressive to me was seeing all the human efforts to contain the virus, but nothing worked until a period of very cold weather knocked out the mosquitoes that carried VEE.

Is there a human vaccine for Venezuelan equine encephalitis?

Because about 30 percent of people who get the VEE vaccine develop pretty bad symptoms, it serves only as a fallback in case VEE would be used in biological warfare. The natural focus is on vaccinating horses, which are more susceptible to mosquito bites. If you stop transmission among horses, you're likely to stop it from spreading to humans.

You kept your promise to earn your Ph.D. from an Ivy League school.

I went to Cornell Medical College because I wanted to study with Dr. William Sherer, the best investigator of VEE at the time. I studied with him for two years until he died unexpectedly. Then, with an arrangement between Cornell and the Centers for Disease Control and Prevention in Colorado, I set up my thesis project at the CDC.

That change in your plans led to an impressive early career with the CDC, where your post-doctoral research produced a major scientific breakthrough.

I worked on polio at the CDC in Atlanta. Polio mutates much quicker than other viruses. So if you want to learn virus genetics, especially how a virus mutates, polio is the best virus to study. Because I had a master's degree in public health and a focus on epidemiology, we developed a method to follow polio strains around the world. If I got a sample from a patient with polio, I could tell you where that virus came from by looking at its genetics. That was important for the World Health Organization's subsequent strategy to eradicate polio. The method we devised helped identify the source of polio outbreaks and establish the pathways of transmission.

For example, there was a polio outbreak in the United States among the Amish community, who do not accept vaccinations. Using the method we'd developed, we showed that the Amish patients in the United States had been infected by a virus originating in the Middle East. We were able to backtrack the original virus to Turkish guest workers who were infected and went to the Netherlands, where they spread the infection to a religious group that was visited by the Amish Americans, who carried the infection back to the United States and Canada. Based on this information, WHO allocated funds to combat polio in Turkey, the source, to prevent further spread of polio to other countries.

This was the first use of what is today called molecular epidemiology, and it led to us getting the Shepard Award for Research Publication by the CDC. The award goes to the best publication of the year by a CDC investigator and is meant to honor CDC employees who author a paper that changes epidemiology or public health practices.

Didn't your work with the CDC also lead to your research on dengue?

When I was a student at the CDC in Colorado, the directors of the Colorado labs and the CDC labs in Puerto Rico decided I should learn how to work on dengue. They wanted somebody well trained who could work in Latin America. I remember telling them, "This is nothing compared to VEE. Dengue is something you can survive."

Then dengue began to spread in Latin America in the 1980s, and soon the number of people infected with dengue totally eclipsed Venezuelan equine encephalitis. So when I was offered an assistant professor position at Yale, I started dengue research.

You were at Yale University for nine years. What lured you to SFBR?

The opportunity to focus on my research, since at Yale, teaching consumed half my time; the fact that SFBR was

building BSL-3 and BSL-4 labs, which I needed for my VEE research; and the fact that San Antonio was closer to dengue. Dengue is already along the Texas-Mexico border, and if it spreads farther into the United States, San Antonio is the likely geographic entry point, along with Houston and parts of Florida. The type of mosquito that is efficient at transmitting dengue is here, and it does well in our climate.

Tell me more about dengue and its public health impact.

Dengue fever is a flu-like disease accompanied by a rash and gastrointestinal problems. It's self-limiting. You recover, but it feels like you have a bad flu for two to three weeks. It's called "break-bone fever" because the severe body aches can make it feel like your bones are breaking. The serious form of the disease, dengue hemorrhagic fever, also causes internal bleeding.

Every year, 50 million to 100 million people around the world get dengue fever. Dengue is prevalent throughout Mexico, which averages hundreds of thousands of cases each year, including 5,000 to 10,000 severe cases. During the last couple of centuries, the United States had periodic outbreaks in Baltimore, Washington D.C., New Orleans, Houston and Galveston. During this century, dengue outbreaks have occurred in South Texas border cities.

What causes the hemorrhagic form of the disease?

For years, the belief was that it depends solely on the number of dengue infections you've had. There are four major types of the dengue virus. After you've been infected with one, you develop immunity to that type, but you can still be infected with the other three. So you can be infected a total of four times. By your second infection, your risk of developing the hemorrhagic fever increases dramatically.

But I published research in 1990 showing for the first time that the strain of the virus also has an impact. One causes more severe disease. We determined this through an epidemiologic study. We obtained samples from dengue patients all over the world and identified the genetic strains of the viruses. Then we did comparisons to see which strains caused epidemics and which didn't, which caused hemorrhagic fever and which didn't. We developed evolutionary trees that told us that all the strains of virus that caused hemorrhagic fever fit into one genetic group.

You've had some other major findings since coming to SFBR in 1996.

In 1997, we published a paper in *Virology* showing how a particular strain of the virus I've been following since 1987 – the more virulent strain – spread around the world from Southeast Asia to Cuba and then throughout South America. In 1999, we published another paper showing which part of the virus is responsible for its greater virulence.

I've continued to follow this strain ever since. It reached Texas in 2005 and caused a small outbreak in Brownsville that November and December. It's bad news that the nasty form of dengue is in Texas. Besides causing more severe disease, it's more efficient at spreading, which we showed in an article in the *Journal of Virology* in 2005.

In the laboratory, we infected human white blood cells with various strains of dengue, and the more virulent strain replicated at 10 times the rate of the others. When we studied this strain in mosquitoes, the animals transmitted it

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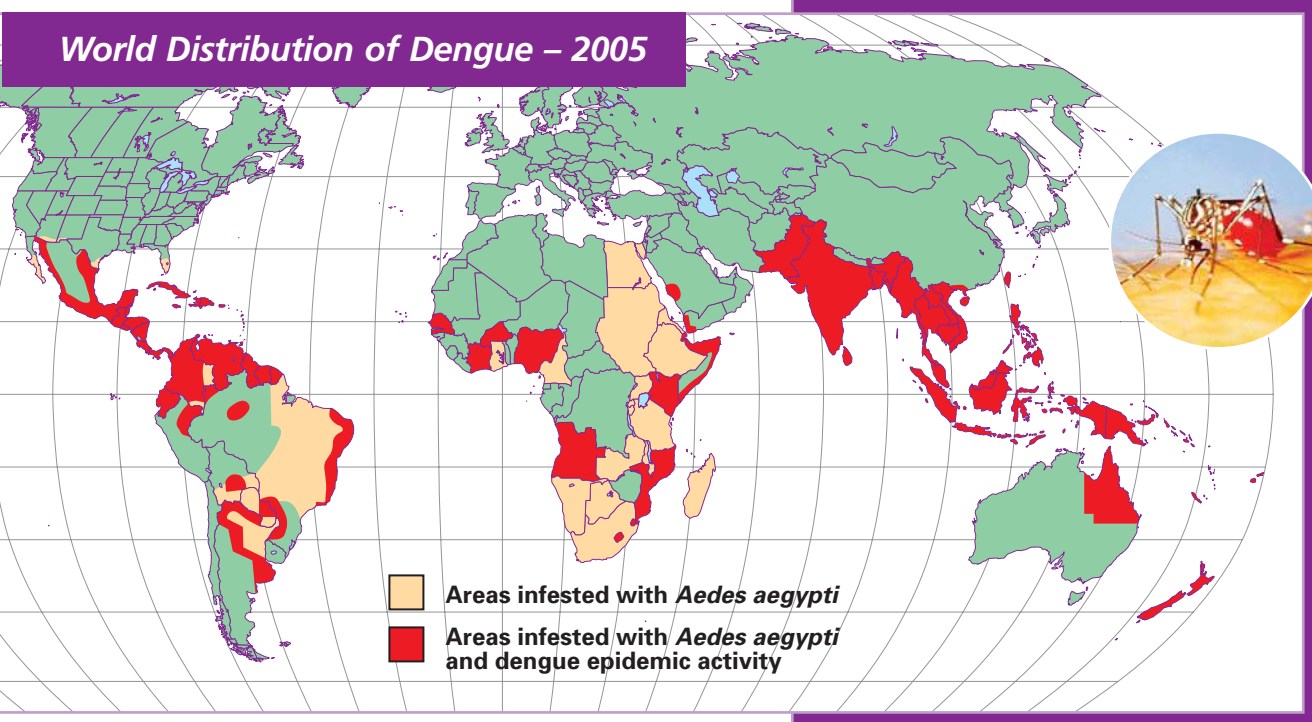
A look at dengue around the world



From the Centers for Disease Control and Prevention

Aedes aegypti, the mosquito that can carry dengue, is recognized by white stripes on its legs and body.

Dengue, like the mosquito that carries it, is found in over 100 countries worldwide, causing dengue fever in 50 million to 100 million people each year, as well as several hundred thousand cases of dengue hemorrhagic fever. Periodic outbreaks of dengue fever have occurred along the South Texas border since the 1980s, and the most virulent strain of dengue, which can cause hemorrhagic fever, was first reported in Brownsville in late 2005.

There is no specific medication for treatment of a dengue infection. Persons who think they have dengue should consult a physician. Treatment for dengue fever typically includes bed rest, drinking plenty of fluids, and use of pain relievers that do not include aspirin. Dengue hemorrhagic fever typically requires hospitalization and can be effectively treated with fluid-replacement therapy if diagnosed early.

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at 65 times the rate of the other strains. This tells me that, with the more virulent strain here, we can expect to see more severe disease in South Texas, and we can expect dengue to spread more quickly.

While this sounds scary for the people of South Texas, you have some good news as well. Tell us how you developed the first animal model for dengue research.

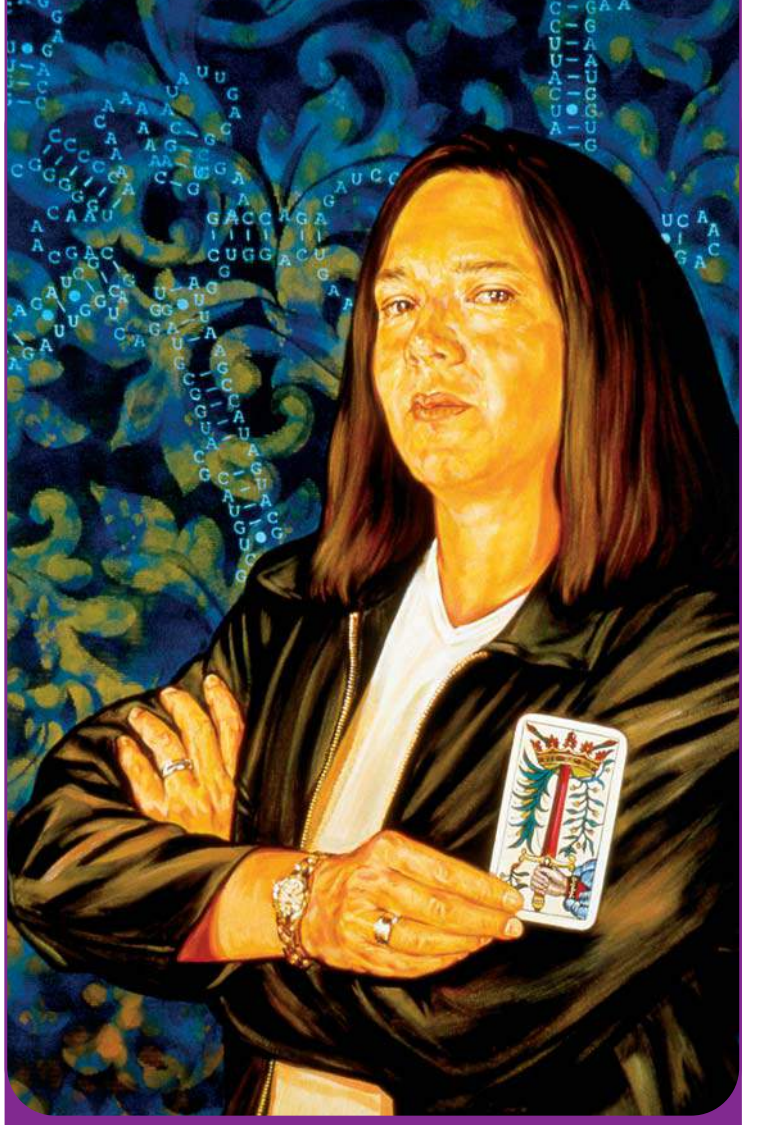
Until now, there has never been an animal model for dengue, because only humans are susceptible. Recently, we saw that some immunologists in Dallas were taking mice that genetically have no immune system, and they were giving the mice transplants of human [umbilical] cord blood cells. Cord blood contains a type of stem cell that eventually forms white blood cells called dendritic cells. They were doing this for cancer research, but dendritic cells are also the type of cells you need to develop dengue. So I got the idea that we might use this same method to develop an animal model for dengue.

With a grant from the Ellison Foundation, we purchased some of these mice. One group we transplanted with human cord blood and then inoculated with dengue. That group developed dengue fever. They had the virus circulating in their blood, they got fever, they even developed a rash. The same did not happen with our control groups. So we knew at last we had an animal model. We published this news in late 2005.

What does it mean finally to have an animal model for dengue research?

The most exciting thing is that it allows us for the first time to test potential antivirals and vaccines in a living system. Until now, they could only be tested on cells in a Petri dish, and that tells you nothing about how a therapy or vaccine will work in a living animal, how it will interact with the immune system, and so on.

Ten companies are waiting to test vaccines, and hundreds want to test antivirals. Several have approached us about conducting these tests. Our limitations are time and money; it takes a lot of each to produce the special mice needed for this research.



Dr. Rebeca Rico-Hesse's love for science and art come together in this portrait by Angel Rodriguez-Diaz. Titling the image "*La Valentina*," meaning, "The Valiant One," the artist uses symbolism to capture Dr. Rico-Hesse's personality and her quest to benefit humanity through dengue research. She holds a card known as the "Ace of Sword," used in the old Spanish card game, *Brisca*, to illustrate her fight against dengue. In the background is the artist's rendition of dengue virus RNA.

The Ellison Foundation provided $50,000 for our pilot study. That tells you about the potential of donor funding, since one gift led to the development of a phenomenal new resource. It also tells you how expensive it is to develop these mice. We've recently applied for NIH funding to develop more of them.

While people are waiting for vaccines and antivirals to be tested, what can they do to prevent the spread of dengue and protect themselves from infection?

We need to prevent mosquitoes from breeding by eliminating standing water, including the bottoms of flower pots, which people often forget. If you have a bird bath, change out the water daily. When people are outside, insect repellants can protect them temporarily – the kinds with DEET are most effective – as can insecticides that are not toxic to the environment. The pyrethrin-based insecticides repel and kill adult mosquitoes. Other mosquitoes will be back the following day, but it's a great idea to spray your yard before you have an outdoor party.

I've heard that when you're not in the lab fighting viruses, you're in a gym practicing martial arts.

I practice a Brazilian form of martial arts called Capoeira. It's not for self-defense, and there is no physical contact. It's more of a dance, even involving musical instruments as well as gymnastics. I enjoy it for the exercise and for the artistry of it.

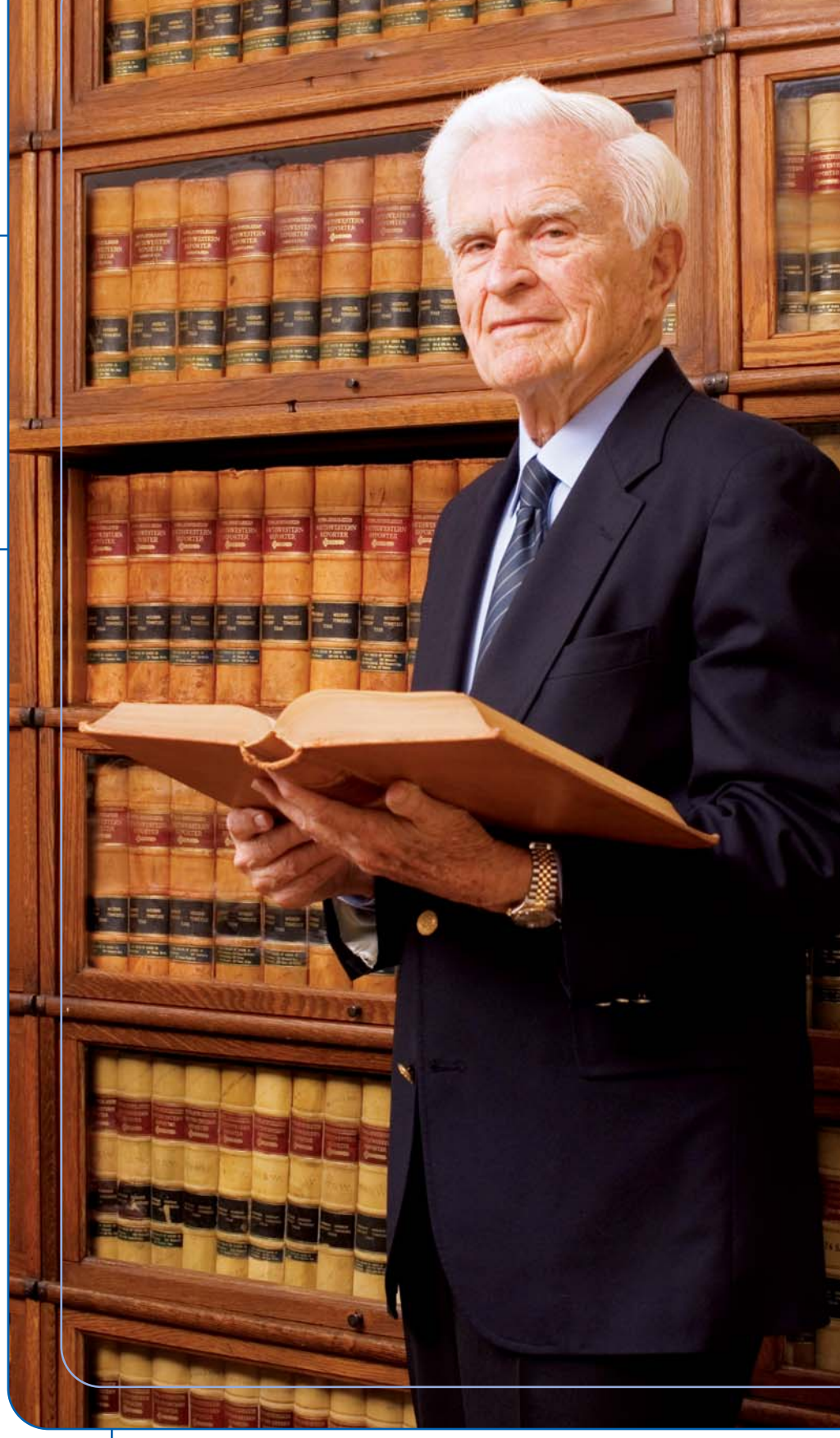
There is an artistic side to you, isn't there?

I picked up my mother's love of art. She was a professional artist and taught at the state university in Coahuila, Mexico, for a time. When she was growing up in Corpus Christi, she won a contest to design the city's flag, which is still used today.

I try to stay on top of the contemporary art scene. I attend a lot of art openings, and most of my friends are artists. I enjoy socializing with them because we have a lot in common. Many people don't realize that science is a creative process. Our research doesn't give us numbers that tell us exactly what it's all about. We have to be creative to understand what we're measuring.

Trustee spotlight:

Leroy G. Denman Jr.



A regular feature of the Progress *magazine is our "Trustee Spotlight," which features our stellar trustees and their valuable contributions to SFBR and the larger community. For this issue, the* Progress *editor visited with Leroy G. Denman Jr., a founding trustee who has remained active with SFBR since he helped Tom Slick establish the organization 65 years ago. One of South Texas' leading attorneys for decades, Mr. Denman has provided counsel to some of the region's most prominent families and businesses while also playing a leading role with numerous philanthropic organizations.*

More than a founding trustee of SFBR, you were a personal friend of its founder, Tom Slick, who asked you to draw up the trust document establishing the organization. Would you share some history of how that came to pass?

When Tom moved to San Antonio, we became fast friends. We were the same age, and he, his wife, my wife and I enjoyed doing things together, including picnic lunches and hikes at our place in the Hill Country. We had a lot of discussions about things he wanted to do, which revolved mostly around the idea of experimentation. He was very imaginative and always looking for new and better ways to do things, whether it be in the oil industry, cattle breeding, construction, mechanics or health matters.

As a very young man, he inherited a large net worth of assets in the oil business in Oklahoma, and he had the idea clearly in his mind that anyone who was wealthy, particularly at a young age, should devote his wealth to the public welfare, as well as to the scholastic life, not just enjoying one's wealth. He particularly wanted to establish a foundation to explore and to develop new things that would be good for humanity.

He asked me to draw the trust instrument that created the Foundation, but I was not his personal attorney. Arthur Seeligson, a relative with his own law firm, served as Tom's legal counsel. But I think he wanted me to draw the trust document because we had already talked so much about what he wanted to do. I understood his plans. Besides that, he probably thought that if he went to an older lawyer he'd be advised not to do it!

In fact, San Antonio was not a hub of scientific research at the time, and many people thought his idea was outlandish. How did you advise him?

World War II was just beginning, and he and I were

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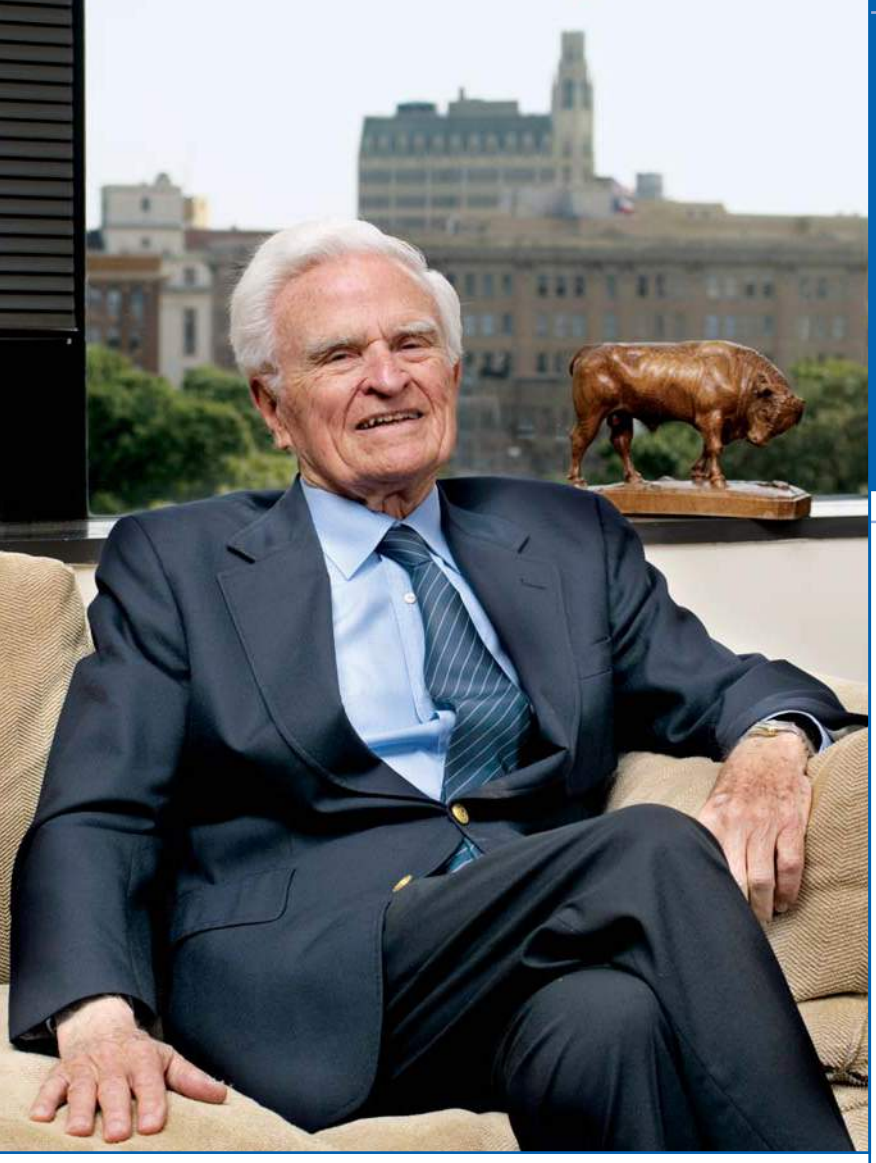

In his downtown San Antonio office, Leroy G. Denman Jr. keeps a sculpture left to him by Tom Slick. Shown here above Mr. Denman's shoulder, the sculpture depicts Mr. Slick's idea of the perfect bull, a subject the two discussed frequently.

Denman, continued from page 15

both living in the shadow of the fact that we had to go to war. Tom kept talking about starting a scientific foundation, and I kept saying, "You'd better wait until after this war. We don't know if we'll live."

He said that was reason to do this right away. I couldn't help but admire him for wanting to devote his fortune to the good of humanity, and I thought it was a marvelous opportunity for people of real scientific ability to come together based on what Tom was able to provide. So I drew up the document.

Then of course we did both go off to war, I with the Foreign Service and he in things connected with the Navy. After the war, things took off. He acquired the old Cable Ranch, recruited scientists to the Foundation, and energetically fostered their scientific studies. Then I had the pleasure of being with him on a formal basis as an advisor and friend to talk about the things he was doing with the Foundation.

What were things like in those early days of the Foundation? Were you and the other trustees very involved, or were things more under Tom's guidance?

Oh, it was mostly Tom. But he did consult with a number of people whom he respected, and he was good at taking advice. In fact, he was not original in how he structured the Foundation. There were other research institutions around the country he admired, and he visited them to learn about their operations and how they recruited scientists. He used what he learned from them to establish a very sound operation.

He loved being at the Foundation, visiting with the scientists, and trying to stimulate them to think in new ways. I think his happiest moments were at a roundtable with a group of scientists, joining in discussions about what might work and what might not work in health matters and mechanical things.

Not all of your dealings with Tom Slick revolved around the Foundation.

No, he was fun to be with, and we did a number of things together. He wasn't one for typical vacations. He looked at travel as a learning experience, and I remember his interest in learning about Mexico. We went to Mexico City together one time. He had heard of a church there where poor people went on their hands and knees a long distance up a mountain to get to that church and receive a blessing from the priest. He was fascinated by the dedication and religious enthusiasm that would impel them to do this.

His interest in cattle also was an exercise. He wanted to know how to breed the best cow. He and I debated what the ideal animal ought to look like, and we argued about whether King Ranch was on the right track in crossing the British breeds with the Indian breed, the Brahman. Tom was a student of genetics, and he believed the genetic pattern of

Leroy G. Denman Jr. (shown near the left-center of this photo, to the left of the fireplace and right of the window) participates in the June 1969 stockholders meeting in the main residence at King Ranch. Around the room are descendants of Captain Richard and Henrietta King.

Photo courtesy of King Ranch Archives, King Ranch, Inc., Kingsville, Texas.

animals was too torn up by going towards the Brahman. He thought you should stay with the British breeds while being directive enough to avoid the frailty of those breeds.

In fact, after he died, I was given a sculpture of a bull with a note from him saying this was what the ideal bull ought to look like. He had had it made, and I believe he had intended to give it to me himself, but he didn't get the chance.

You obviously had a different idea about the perfect bull. What was your line of thinking?

I preferred what King Ranch was doing, devising a fine animal that could withstand dry areas and harsher environments. My other exercise in life was with Bob Kleberg, who designed the Santa Gertrudis breed, a mixture of Brahman and Shorthorn breeds. Santa Gertrudis was the name of the land grant for the first land Captain King bought when he came to Texas. King Ranch is properly called the Santa Gertrudis Ranch; at least the headquarters division is.

How did you come to be the lead attorney for King Ranch?

My father represented Mrs. King's immediate family when they were in the process of establishing the ranch. I carried the briefcases for all those things for years, and in the process became acquainted with Bob Kleberg and his brother Dick. When my father died, I was a fairly young attorney, in my 30s, but Bob trusted me. He thought I was ready to do what was needed, so I served as the lead attorney for 50 years, during the time he was building up their foreign operations.

Bob thought he had developed a method of ranching and a breed of cattle that could do well in many places of the world. So when they discovered oil on King Ranch and had surplus money, he devoted it to buying and setting up ranches in different parts of the world: Cuba, Venezuela, Brazil, Argentina, Spain, Morocco and Australia.

Our plan was that I would go with him and watch him pick out a tract of land he thought was suitable. Then he would move on and leave me behind to negotiate the deal and make the purchase. Often I was out in the middle of nowhere, and it could seem like I'd never make it back. He laughed at a letter I wrote him from the Australian Outback one time. It started, "Bob, I'm writing you this letter, but I doubt it will ever get to you."

It sounds like you and Bob Kleberg had some fun adventures.

He was the most imaginative person I've ever known. He conceived the idea of a worldwide cattle business – going into areas that had a seed of a cattle industry but where that industry was underdeveloped, places where the industry was needed both to feed the people of that country and create an export business – and he was imaginative enough to paint the right picture to sell the idea to some foreign governments that were feudalistic in their thinking. He was persuasive. He could sell you anything. But it was a good thing he was persuading these governments to do, developing a resource for their country.

With his resources and experience, he was able to do a lot for these countries. One example is Australia, where he leased 4 or 5 million acres from the government. You can't find a much harsher environment than the Outback. The Australians' theory was, "If a cow can't walk 10 miles to water, too bad." Bob insisted that they had to have more water, and then he helped them dig deeper water wells than they were used to drilling.

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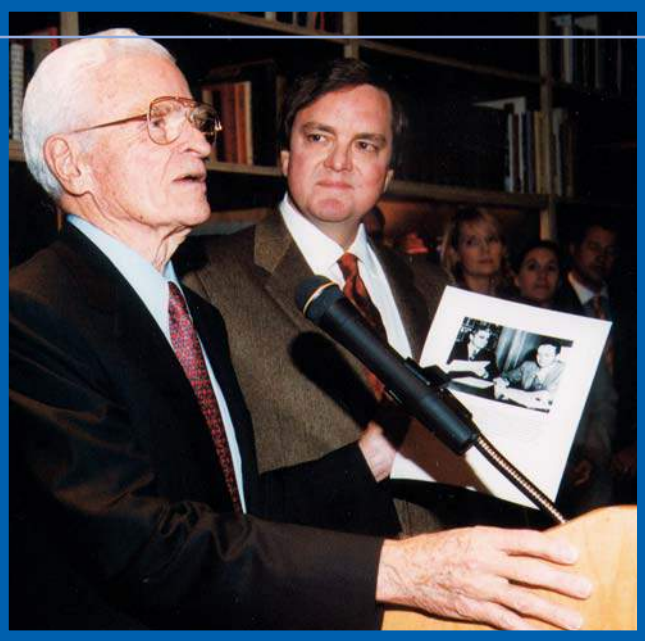


Leroy G. Denman Jr. and Bruce Bugg, trustees for the Tobin Endowment, share some SFBR history with Founder's Council members during the group's holiday party at the Tobin Estate.

Tom Slick signs documents related to SFBR's founding as Leroy Denman looks on.

Denman, continued from page 17

You still serve on the Board of Directors for the Caesar Kleberg Foundation for Wildlife Conservation. Is that because of your closeness to the Kleberg family?

Mr. Caesar [Kleberg] was a wonderful inspiration to me as a child. He was a wonderful man to have at King Ranch, where he was always a leveling influence. But I remember him so fondly from my childhood, when he would come into town to discuss legal issues with my father and have dinner at our house. He was very kind to me, even giving me a little dog and taking time to help me teach it its name.

The Caesar Kleberg Foundation devotes itself to supporting agricultural research and education. As has happened with so many of my other clients, the family established a foundation and named me a trustee. I spend most of my time these days trying to help those foundations spend their money in the way their founder, or the person for whom the foundation is named, would have wanted.

That's the case with the Tobin Endowment, where you also serve as a trustee. It does a lot for the arts, among other important initiatives, and it's followed the Tobin family in being a good friend to SFBR. Didn't Margaret Tobin house the Foundation's first baboons in her barn before their permanent housing was built?

That's right. That was Margaret Batts Tobin, daughter of Judge Batts, and wife of Edgar Tobin. He started an aerial survey mapping business for the oil industry, working in Texas, Oklahoma, Louisiana and even New Mexico. My father did legal work for Mr. Tobin until he (my father) became ill. Then Edgar took me on to help him with the legal aspects of his business. When he was killed in a plane crash, Mrs. Tobin sent me to tell their son, Robert, who had just left for school at the University of Texas.

Robert and I became fast friends after that, and I continued to provide legal counsel for the Tobins and the family survey business, along with Robert's friend, Bruce Bugg, then a young attorney. After his mother died, Robert had us arrange the sale of the business. In his will, he established the Tobin Endowment and named Bruce and me as trustees. Today, we try to support his interests. Robert loved music, opera and the arts. He spent a lot of his time with children, too, trying to educate young people, and he was a great supporter of the local children's shelter. Bruce and I recently toured some properties the endowment has helped the shelter develop.

Leroy G. Denman Jr.'s office reflects his legal career and the clients he has served. In the background are maps of clients' ranches and oil and gas leases. In the foreground is a desk that once belonged to George Brackenridge, a client of his father. Mr. Denman continues to serve as a trustee for the Brackenridge Foundation.

Through your involvement with these foundations and others, such as the Brackenridge and Ewing Halsell Foundations, you've had the opportunity to have a positive influence on so many areas of society. It must be very fulfilling.

With all these, my work is to pursue the things that the testator who named me thought worthy of pursuit. I've done the best I can, and it's been an honor.

The Tobin Endowment made a large contribution toward recent renovations in the Earl F. Slick Center at SFBR. In recognition of that gift, and in honor of a request Robert Tobin once made that Bruce Bugg find an appropriate way to honor you, a beautiful new atrium in that research complex is being named for you. What does the dedication of the Denman Atrium at SFBR mean to you?

I feel like it's a great tribute I don't deserve, because while I was there early on and certainly tried to help the Foundation in a lot of things, other people have devoted their lives to it. But of course I'm gratified that they chose to name that room for me.

You've accomplished much as an attorney, following in the footsteps of your grandfather, Leroy G. Denman Sr., former associate justice on the Texas Supreme Court, and your father, Leroy G. Denman Jr., with whom you served some of South Texas' most distinguished clients. What have you enjoyed most about your career?

The practice of law, starting with graduation from law school in 1939 and being a lawyer ever since. I've been blessed with wonderful clients who had things for me to do that were interesting and who entrusted me with their dreams, whether it be a ranch or a survey business or a publishing company. Being associated with successful people is as good as a law practice can get.

New legislation makes lifetime gifts easier

Did you know that the Pension Protection Act of 2006 allows individuals age 70½ or older to use IRA accounts to make gifts during their lifetime without any undesirable tax effects? Prior to the new law, you would have to report any amount taken from your IRA as taxable income, then take a charitable deduction for the gift, but only up to 50 percent of your adjusted gross income. In effect, this caused some donors to pay more in incomes taxes than if they had not made a gift at all.

Fortunately, through Dec. 31, 2007, these IRA gifts can be accomplished easily and without unnecessary tax complications. Plus, you can make the gift to a qualified organization – excluding charitable trusts, donor-advised funds or supporting organizations – while you are living and able to witness the benefits of your generosity.

To be eligible for the special tax treatment, you must be at least 70½ years old on the day you make the gift. The maximum amount you can give from your IRA is $100,000 in 2006 and $100,000 in 2007. If desired, your spouse, if 70½, can also give $100,000 per year from his or her own IRA. In addition, if you do not need your required minimum distributions, you can transfer those payments directly to an eligible organization such as SFBR, and you will not have to pay income tax on the required distributions as long as your IRA gifts total $100,000 or less for the year.

You can make such a gift to SFBR simply by contacting your IRA custodian to make a direct transfer from your IRA to SFBR. Be sure to have the IRA custodian send the funds electronically or by a check made payable to the charitable organization. If the custodian makes the check payable to you, and you deposit it into your bank account and write a personal check for the charitable gift, you will not be eligible for the special tax breaks.

This is a unique way to create an endowment fund at SFBR or to benefit one of your favorite areas of research. If you would like to discuss a gift using this or any other tax-advantaged method, please call Corbett Christie, SFBR's chief development officer, at 210-258-9870.

This information is not intended as legal advice. For legal advice, please consult an attorney.

Frazier joins SFBR as new CFO

Southwest Foundation for Biomedical Research is pleased to welcome Jeannie Frazier as the organization's new chief financial officer.

Frazier, who joined the SFBR management team on Nov. 6, brings a depth of experience to her new position, having worked for 24 years in the financial management of health care and research organizations.

Most recently, she served as CFO for the Cancer Therapy & Research Center, managing the finances of one of the pillars of San Antonio's biomedical economy. Previously, she held key management positions in both for-profit and not-for-profit health care organizations in Houston, where she served as senior vice president at Mischer Healthcare, as CFO for Hermann Hospital, and as director of Operations Research for the Sisters of Charity Health Care System, which later was part of a merger that formed CHRISTUS.

She holds both a master of science in engineering economic systems and a bachelor of science in mathematical sciences from Stanford University.

"We are delighted that Jeannie has decided to bring her skills and expertise to Southwest Foundation for Biomedical Research," said John C. Kerr, president and chairman of SFBR. "Her extensive experience in senior management of large biomedical research and health care organizations in both San Antonio and Houston make her uniquely qualified for this important position at SFBR. She's a great asset to San Antonio."

Frazier says she has been impressed by the work of SFBR and looks forward to supporting its important mission. "Since my move to San Antonio, I've been struck by what a dynamic and innovative place Southwest Foundation for Biomedical Research is," she said. "I consider myself a math-science person at heart, so I'm excited by this opportunity to use my skills in support of the organization's amazing scientific efforts."

In fact, she says support is what her job is all about. "My attitude about finance and all of administration is that we're a support department," she said. "Our goal is to take care of our customers, with our customers being the internal departments of SFBR that rely on our services, as well as the SFBR Board of Trustees and all the external users of our financial statements. If we're not making our customers happy, then we're not doing a good job."

Frazier believes her extensive not-for-profit experience, coupled with the knowledge she has gained at CTRC about the highly competitive area of grant-funded research, have prepared her well for her new position at SFBR. "I see this as an opportunity to use what I've learned to build on the strong foundation at SFBR, while bringing some new ideas that I hope can help make the organization even stronger," said Frazier. "I'm thrilled to be part of the SFBR team."

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 Argyle, the Southwest Foundation Forum, and the Founder's Council.

The Golden Circle

Members of the Golden Circle, Benefactor Circle, President's Circle, and Chairman's Circle are among SFBR's closest friends and supporters. Each year, they make contributions of $1,000, $2,500, $5,000 and $10,000, 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 life-saving research projects.

To thank our partners in progress for their generosity, SFBR hosted a Golden Circle dinner at The Argyle on Oct. 23, featuring SFBR President and Chairman John C. Kerr as keynote speaker. Mr. Kerr described for guests the dedication he's seen by SFBR faculty and staff since stepping into the role of president in June, the strong position SFBR holds in terms of scientific excellence and financial stability, progress made in fine-tuning the organization for the benefit of future achievement, and recent achievements by SFBR scientists.

The evening was a celebration of past accomplishments and hopes for even greater future success in the mission to improve human health through innovative biomedical research. Some memorable photos from the evening are provided on the following page.

If you would like to become a partner in scientific progress through membership in the Golden Circle, fill out and return the form provided on this page, or contact Corbett Christie, SFBR's chief development officer, at 210-258-9870. You also can learn more about the Golden Circle and join online at http://www.sfbr.org/pages/support_circle.php.

To speak with Corbett Christie about giving opportunities, contact him at 210-258-9870 or cchristie@sfbr.org.

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.

Clip and mail this form to: SFBR
Attn: Development Office
P.O. Box 760549
San Antonio, TX 78245-0549

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

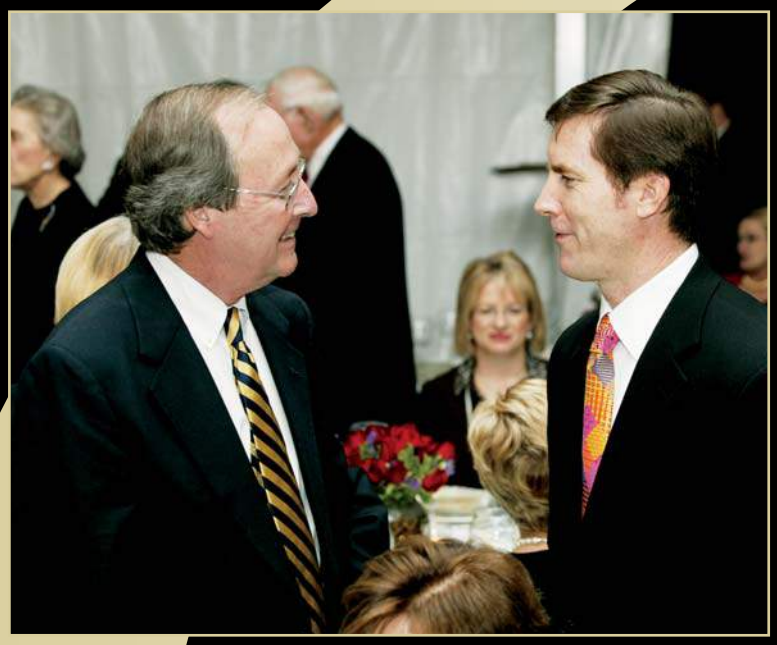
_____
Billing Address

_____
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.***

Golden Celebration



Southwest Foundation Forum

Kathryn Dehlinger, the Forum's 2005-2006 president, signs the check for this year's Forum grant awards to SFBR scientists, funded with proceeds from the 2006 Gala.

Estee Kellogg and Caroline Schupbach, co-chairs of the 2006 Gala, prepare to welcome guests to the event.

Guests enjoy the Forum's 2006 Gala, which turned out to be the largest fundraiser in the group's history.

Celebrating a banner year

The Southwest Foundation Forum started off its 2006-2007 year by making its largest donation ever to SFBR, thanks to the astounding success of its spring gala.

On hand for the occasion Sept. 6 were 2005-2006 Forum President Kathryn Dehlinger, 2006 Gala Co-chairs Estee Kellogg and Caroline Schupbach, and Forum 2005-2006 Advisor Nancy Moorman, who presented SFBR President and Chairman John C. Kerr with a check for $155,000.

This spectacular gift resulted from the hard work and ingenuity of the gala organizers and volunteers, as well as the generosity of numerous gala sponsors, including lead sponsors AT&T, the Mays Family Foundation, and Valero Energy Corp. Special thanks also go to Tiffany & Co, which provided guests with beautiful party favors.

"This donation from the Forum is truly outstanding," said Mr. Kerr, "and it means so much to our scientists. Already encouraged by the Forum's enthusiastic support of scientific research, more of our scientists than ever will benefit this year from a Forum-sponsored pilot study grant. Based on novel ideas, pilot studies provide the basic scientific data to show that a scientist's new idea has merit. That data is then used to leverage larger funding from granting institutions such as the National Institutes of Health. So in reality, this check is worth many times its face amount."

For more information on how this year's Forum gift will benefit specific SFBR scientists and their innovative research programs, see the article beginning on page 23.

In a separate donation made this summer from proceeds generated through other Forum activities, the group gave $13,000 to SFBR for the purchase of audio-visual equipment. This equipment will be used in a conference room of the Earl F. Slick Center, scheduled for dedication in February. There it will benefit SFBR scientists and administrators campus wide as it is used for meetings, teleconferences and presentations.

Never ones to sit idle, Forum members are now in the middle of another action-packed year. On Sept. 27, they went "Shopping for a Cause" at Julian Gold. Every ring of the cash register was good for science, as Julian Gold returns 10 percent of the evening's proceeds to the Southwest Foundation Forum in support of its mission.

On Oct. 25, the Forum brought a crowd to the Foundation to enjoy a reception and campus tour, complete with compelling presentations by SFBR scientists. Featured this year were Dr. Rebecca Rico-Hesse and her research on dengue fever; Dr. Eric Moses and his research on preeclampsia, the most common major disorder of human pregnancy; Dr. Andrew Hayhurst and his research in biodefense; and Dr. Laura Almasy, who uses statistical methods to find genes influencing our susceptibility to heart disease, stroke, schizophrenia and drug dependence.

In November, the Forum had a packed house for its Fall Lecture Luncheon featuring Dr. Jean Patterson. Speaking on "Avian flu and bioterrorism: Should I ever leave the house?," Dr. Patterson kept the group captivated – as well as inspired to continue their support of the Foundation's biodefense initiatives!

Now the group is gearing up for a busy spring, complete with student tours of SFBR, science education awards to area schools, a Spring Lecture Luncheon, and its 2007 Gala. For more information on Forum activities and membership, log onto www.swff.org.

‘Run for the Roses’ produces large payoff for human health

The Southwest Foundation Forum’s “Run for the Roses” Gala – held in May with a theme based on the Kentucky Derby – produced a spectacular prize to help scientists in the race to prevent, treat and cure disease. This year’s event was so successful that it allowed the Forum to donate a record-setting $155,000 to Southwest Foundation for Biomedical Research to support innovative new research projects.

Presented to SFBR President and Chairman John C. Kerr on Sept. 6, this donation will be used by the Foundation to fund the following six new pilot studies.

How obesity affects our immune system

Dr. J. Michael Proffitt in the Department of Genetics received a Forum grant to study the relationship between obesity and disease by examining the effect of different types of body fat on the immune system. For example, as part of his new project, he will explore the relationship between immune cells and fat cells in obese and lean baboons. He hopes to identify which immune cells participate in inflammation associated with obesity and how the immune system functions differently in the lean and obese state – all part of his overall goal of helping the research community develop appropriate therapies to mitigate the damage caused by fat tissue and to help physicians better manage obesity-related illnesses such as diabetes and cardiovascular disease.

What makes some strains of herpes deadly?

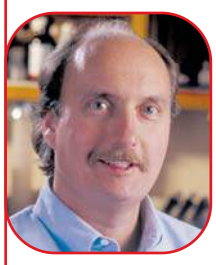
Dr. Anthony Griffiths in the Department of Virology and Immunology focuses his research on different types of the herpes virus. Herpes simplex virus (the cause of cold sores) – to which most people are exposed by adulthood – is usually self-limiting and not life-threatening. On the other hand, herpes B virus is one of the most dangerous human pathogens known, causing death in 70 percent of those infected.

Dr. Griffiths is trying to discover what differences in these two similar viruses are responsible for the difference in the type and severity of disease they cause in humans. That understanding could lead to improved treatments and therapies. With his new Forum grant, he will begin investigating a newly discovered class of molecules called microRNAs, particularly focusing on several that he predicts play a role in the pathogenesis of herpes B virus.

Another step forward in biodefense

Another Forum grant to the Department of Virology and Immunology was awarded to Dr. Ricardo Carrion Jr. His grant will be used to develop the common marmoset monkey as a research model for Ebola virus. An emerging virus that causes outbreaks in Africa every two to 10 years, this hemorrhagic fever virus has a fatality rate of 60 to 90 percent and is a potential bioterror threat. Development of the marmoset as a research model will be highly beneficial to research studies on the efficacy of candidate vaccines and therapeutics for Ebola.

The genetics of psychiatric illness



Dr. Jeff Rogers in the Department of Genetics will use his new Forum grant to expand his research with baboons on the genetics of psychiatric disease and take that already productive research in a new direction. Research by him and his collaborators already has shown that genetic variation in baboons influences their response to mild stress; affects the frequency of aggressive, submissive, and anxiety-related behaviors; and impacts levels of serotonin, dopamine and norepinephrine, three brain chemicals known to be involved in the onset and treatment of human depression and anxiety disorders. Dr. Rogers’ ability to find the particular genes affecting these various traits would be greatly enhanced if he knew which regions within the baboon brain are affected by the genes for which he is searching.

Therefore, his new grant from the Forum will be used to conduct a series of brain imaging studies to help him identify related differences in brain structure among baboons in his investigation. Eventually, he hopes to produce findings on the genetic causes of variation in brain anatomy, structure and function to accelerate progress toward a more complete understanding of the genetics of human psychiatric illness. That could lead to better treatment and preventions for psychiatric disease.

The genetics of a serious pregnancy disorder

Preeclampsia is the most common serious disorder of human pregnancy, responsible for approximately 76,000 maternal and infant deaths each year. A rapidly progressive

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The Founder's Council

Having fun searching for a cure

With presentations on such diverse topics as beautiful plants and deadly bugs, the Founder's Council schedule for 2006 has had a healthy mixture of stimulating science and fun.

For a virtual tour of SFBR with a southern summer flare, council members and their guests gathered on the lawn of The Argyle on May 17. As they sipped drinks, dined on delicious appetizers and socialized with friends, they made their way around to visit with brilliant SFBR scientists who were on hand to discuss their ongoing research – complete with clips of television news coverage of their research and conversation-starting props set up at various tables.

Dr. Susan Mooberry and Evelyn Jackson showcased a variety of Texas plants as they discussed their use of these plants in a novel cancer drug discovery program. Just a few steps across the lawn, Drs. Ricardo Carrion Jr. and Andrew Hayhurst displayed a spacesuit worn in SFBR's BSL-4 laboratory, helping council members visualize what these scientists' work is like as they develop and test candidate vaccines and treatments for potential bio-terror agents.

Drs. John Blangero and Laura Almasy rounded out the all-star scientific line-up, discussing how novel statistical methods and computer software designed at SFBR are used in complex genetic analyses to detect disease-influencing genes. Many thanks go to Frost Bank, the event sponsor, for making this special evening possible.

In July, members gathered at The Argyle once again, this time for a lecture luncheon featuring SFBR geneticist Dr. Anthony Comuzzie. At this interesting event sponsored by Dr. Terive Duperier and Weight Wise Bariatric Program, members and guests ate delicious, diabetic-friendly ice cream provided by Dolce Foods – enjoying all the flavor minus the guilt – as they heard Dr. Comuzzie discuss the dangerous cluster of obesity, diabetes and heart disease, along with their precursor, metabolic syndrome. As part of his talk, Dr. Comuzzie described a collaborative study in Houston, in which he and his colleagues are examining genetic influences on these conditions in children.

In the fall, just after the five-year anniversary of the terrorist attacks of Sept. 11, 2001, and near the beginning of flu season, members gathered for a lecture luncheon with Dr. Andrew Hayhurst, who is using antibody engineering techniques to develop improved methods for detecting and defeating SARS and various bio-threat agents. Goldman Sachs was the generous sponsor of this timely event.

In between all these informative activities, the council had time to get together just for fun at two membership appreciation receptions. Hats off to Paloma Blanca Mexican Cuisine for providing the great atmosphere and delicious food that made these gatherings such a success.

Council members learn about Dr. Susan Mooberry's hunt for new cancer drugs among Texas plants during their Virtual Tour of SFBR at The Argyle.

Enjoying social time at recent lecture luncheons are: Above: Ed Hart, Dr. Andrew Hayhurst (guest speaker), and Liesl and Don Noble.
Below: Sharla and Jacob Gray and Kirk Oden.

Stay tuned for the highlight of the Founder's Council year. This year's Holiday Party will be held on Dec. 6 at the Tobin Estate and will feature several grant awards to SFBR scientists. For more information on this members-only event – or to learn how you can become part of the Founder's Council – contact Amy Abdalla at 210-258-9409 or amy@sfbr.org, or log onto www.sfbr.org/pages/founder_council.php.

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condition that leads to high blood pressure and other systemic problems in the latter half of pregnancy, it typically resolves after the baby is delivered. In some cases, it leads to eclampsia, a convulsive condition that is life threatening for the mother and her unborn child. While no preventions or therapies exist for preeclampsia and eclampsia, and while little is known about what triggers their onset, it is clear that genetics play a major role. So the discovery of genes that influence susceptibility would be highly beneficial in efforts to develop diagnostics, preventions and treatments.

A Forum grant to Dr. Matthew Johnson in the Department of Genetics will be used to obtain a complete profile of gene regulatory mechanisms in a sample of unrelated Norwegian women. By simultaneously assessing every gene in the human genome, his project aims to identify and characterize significant differences in the biological relationship of gene regulation between pre-eclamptic and normal pregnancies.

Battling the drug resistance of the schistosome parasite

Schistosome parasites infect and reduce the quality of life of over 200 million people around the world, particularly in developing countries. While there are treatments available, infection frequently reoccurs, and treatments become less effective as the parasites develop increased drug resistance.

Dr. Charles Criscione in the Department of Genetics is trying to locate schistosome parasite genes that underlie drug resistance so that existing drugs can be modified to restore their efficacy. In this effort, a grant from the Forum will be used to help Dr. Criscione develop a new, less cumbersome method for measuring drug resistance in schistosome parasites. If he and his colleagues can develop a simple method for this procedure, they will be able to measure drug resistance in the parents and offspring of a genetic cross between parasites, which would in turn help them locate the genes that cause drug resistance.

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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.

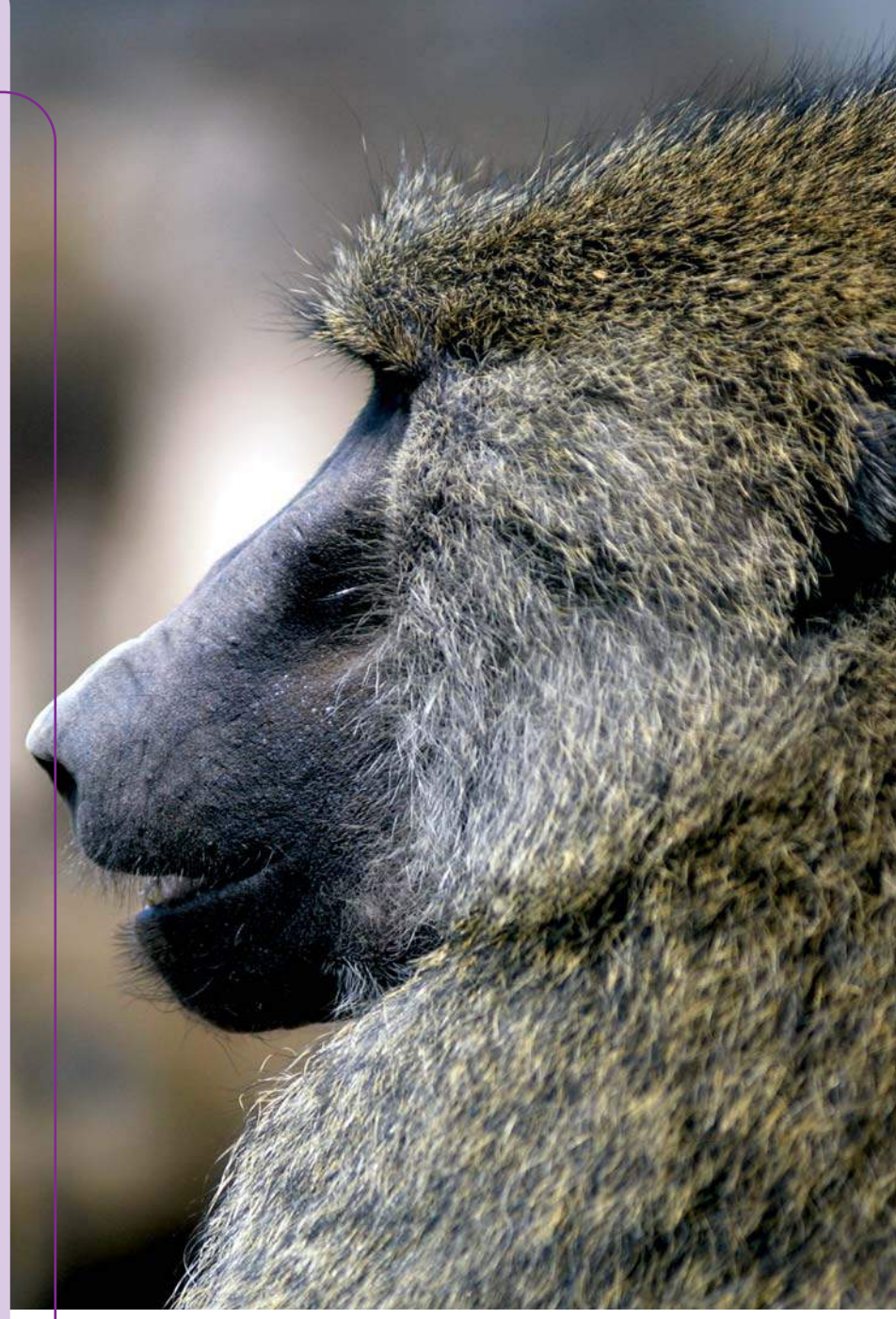
Located on a 332-acre campus in San Antonio, Texas, Southwest Foundation partners with hundreds of researchers and institutions around the world, targeting advances in the fight against heart disease, diabetes, obesity, cancer, hypertension, psychiatric disorders, AIDS, hepatitis, malaria, parasitic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

Other extraordinary resources at SFBR include the nation's only privately owned BSL-4 laboratory, a critical asset to research related to biodefense and emerging infectious diseases, and the AT&T Genomics Computing Center, which houses the world's largest parallel computing cluster for genetic 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 advancing the health of our global community through innovative biomedical research. For more information, please contact the Foundation at 210-258-9400, or visit our Web site, www.sfbr.org.



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