

SFBR

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A Call for a Cure

*A heartwarming struggle against the
heartbreaking disease cystinosis*

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Message from the President

John C. Kerr



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As you read through this issue of *Progress*,

I believe you will see the emergence of a common theme: the vital partnership of you, our friends and donors, in our scientific success.

Time and time again, you will read about a groundbreaking finding, the establishment of a highly novel research program with breakthrough potential, or the awarding of a major federal research grant, and you will notice that at some critical point in the process, donors played a key role.

Our lead article is a compelling example. After two of their grandchildren were diagnosed with a heartbreaking genetic disorder called cystinosis, Dianne and Richard Azar put their financial resources behind the ingenious minds of Drs. John Blangero, Eric Moses and other SFBR geneticists, funding a major research program so novel that it likely would not have been eligible for a federal grant. The results have been astounding, yielding advances with broad application to numerous health issues and spawning a series of new federal grant applications.

The "never-been-done-before" approach SFBR geneticists developed for the cystinosis project is expected to become a new paradigm for the study of single-gene disorders as well as complex diseases that involve multiple genes. Already it has led to discoveries that offer new hope not only to cystinosis patients and their families, but also to people around the world who suffer from or are susceptible to a wide variety of complex diseases.

Funding from the Azars also enabled the development of a new genetic research resource that facilitated a major scientific advancement recently published in the prestigious scientific journal *Nature Genetics*. Drs. Harald Göring, John Blangero, and a team of other SFBR scientists used this resource as the foundation of a groundbreaking genetic research method, and then they used that new research method to identify a gene that regulates HDL cholesterol. As they learn more about the function of this gene, they see that it has implications not only for cardiovascular disease, but also for Alzheimer's, Huntington's, cystinosis, and many other disorders.

In both of these *Progress* articles, you will notice that the Foundation's AT&T Genomics Computing Center served as a vital discovery resource. Recently, a \$1 million grant from the AT&T Foundation enabled a dramatic upgrade of that important resource, doubling the center's computing capacity. With 3,000 processors working in parallel, this facility is now 2.5 times the size of any of our competitors, allowing our geneticists to combine brute computing force and the finesse of analytical software to search for disease-influencing genes with unprecedented speed.

Coupled with a gift from the Elizabeth Huth Coates Charitable Foundation for a new state-of-the-art genetics sequencer – an amazing piece of laboratory equipment that can do in one week what it took the Human Genome Project six months to accomplish – the power of the AT&T Genomics Computing Center is allowing our geneticists to ride the next great wave of genetic research: whole or nearly whole genome sequencing studies. Few places in the world have the resources and expertise to conduct this type of research, but thanks to donor support and scientific ingenuity, SFBR is one of those places. The payoff is expected to be tremendous for human health.

In addition to the important role that donors can play in supporting scientific breakthroughs and funding state-of-the-art technology, they also play a vital role in sponsoring pilot studies. Don't miss articles about major pilot study grants by the Max and Minnie Tomerlin Voelcker Fund and the Southwest Foundation Forum. These early-stage investigations are needed to test innovative, sometimes high-risk/high-reward research and provide concrete results that scientists can use to garner larger federal research grants from the National Institutes of Health and other sources.

And speaking of donor gifts leading to major grants, be sure to read about a new \$1.5 million grant SFBR virologists recently received from the Department of Homeland Security to study the Marburg virus, a potential bioterror weapon. SFBR is one of the few places that can study this and many other deadly pathogens because of our maximum containment laboratory. Built mostly with donor funds, along with support from the NIH, our virology complex is home to the nation's only privately owned spacesuit laboratory, a facility that has placed our scientists at the forefront of biodefense research.

It is exciting to see the increasing impact of philanthropic-scientific partnership, along with what appears to be a new trend in donor-supported research. Individuals, groups and private foundations continue to make important contributions toward traditional sources such as endowment, laboratory equipment and the construction and renovation of facilities, but more and more, they also are willing to step forward and sponsor innovative new research projects, be they pilot studies or major new programs like our cystinosis project. This is crucial to an independent research organization like ours, especially at a time when the lifeblood of basic research – federal funding through the NIH – is experiencing funding cuts.

So I thank our many friends for your generous support. I hope you enjoy reading about some of the fruits of your gifts.



A call for a cure

“I just got the phone call.”

Kim Shepperd, pregnant with a baby girl, froze just long enough for her heart to leap to her throat and brace itself for utter elation or sheer despair. Her husband John’s next words would tip the balance.

“She has it.”

“It.” Cystinosis. The same genetic defect that ravaged the Shepperd’s then 4-year old son. The same cystinosis that already ruled every hour of every day of the lives of Kim, John and their boy, John Ben, with a regimen of medications that barely keeps the disease at bay.

The Shepperds already knew too well that living with cystinosis in the family is to live with a slave driver that demands absolute obedience:

- Every six hours, a drug so foul-tasting that most children must take it through a special tube affixed to their stomach;
- Ten times a day, special eye drops to keep crystals from forming in your child’s eyes and threatening potential blindness;
- About 32 medications a day given to a little boy who first showed symptoms by screaming with thirst, then throwing up water minutes after drinking it.

Now, cystinosis would make the Shepperds’ lives exponentially more challenging. They would soon have a second child, a precocious girl named Ava, after her

► *Continued on page 4*

Cystinosis is a rare metabolic disease caused by a defective *CTNS* gene that fails to transport cystine out of cells. As a result, this amino acid accumulates to toxic levels and forms crystals in the kidneys, eyes, liver, muscles, pancreas, brain and white blood cells.

A Call for a Cure, continued from page 3

grandmother, who like her brother would enter the world already in the grip of the disease and requiring her own inflexible schedule of essential medications. A disease that normally strikes perhaps one child in 150,000 had now hit the Shepperd family twice.

The news hit Kim Shepperd hard. “I just crumbled,” she recalls.

‘We’ve got to do something’

That night, Kim’s parents, Dianne and Richard Azar, made a decision. “We’ve got to do something,” Dianne recalls the two of them agreeing, not even beginning to think their burning desire to help their grandchildren would lead them to a world-renowned genetics research team in their own backyard.

What happened next is the stuff of movie scripts that test the limits of believability. A couple of weeks after the family learned of baby Ava’s cystinosis, a late Friday afternoon call came into Richard Azar’s office. It was Amy Abdalla of the Southwest Foundation for Biomedical Research’s Development Office, calling to thank the Azars for their longtime commitment to SFBR’s Golden Circle of benefactors.

“It was the end of the day on a Friday and I was just about to leave the office,” Azar says, “but something told me to take the call.”

A casual conversation soon turned serious. “Do you all do any research on cystinosis?” he asked.

Abdalla wasn’t sure. She’d never heard of cystinosis.

So Azar proceeded to explain the disease and how it impacts his family.

Cystinosis is a rare metabolic disease caused by a defective *CTNS* gene that fails to transport cystine out of cells. As a result, this amino acid accumulates to toxic levels and forms crystals in the kidneys, eyes, liver, muscles, pancreas, brain and white blood cells.

Without specific treatment, children with cystinosis develop end-stage kidney failure at approximately age 9. Even for individuals who carefully follow the lifetime treatment, kidney disease and the eventual need for a kidney transplant are common. Other complications can include failure to thrive, muscle wasting, difficulty breathing, diabetes, hypothyroidism, ocular problems such as photophobia, or eye pain caused by light, and excessive thirst and urination coupled with episodes of dehydration.

Because cystinosis is so rare – there are only about 400 diagnosed cases in the United States and 2,000 worldwide – it is not well understood or highly studied. In fact, only one pharmaceutical company makes the medication to treat it.

Azar explained that both parents must have a copy of this recessive genetic defect in order to pass this disease to their children, and even then, the odds are only one in four that a child of theirs will actually contract the disorder. So Kim and John Shepperd had “beaten the odds,” so to speak, by having two children with cystinosis. Now the Azars were committed to helping their grandchildren overcome all odds and win the battle against it.



It’s amazing to think that we could be part of

something that could potentially help thousands of people affected by cystinosis and millions affected by other heartbreaking diseases.”

– Kim Shepperd



With a hopeful spirit and a determination to master cystinosis rather than be mastered by it, the Shepperds make family life fun and joyful. Enjoying playtime are (clockwise) John, Kim, Ava, and John Ben Shepperd.

More than 'something' gets done

Following up on Azar's inquiry, Abdalla contacted SFBR's Genetics Department, where scientists are known for their expertise in hunting down genetic contributions to common complex diseases such as heart disease and diabetes. The response she got? The department didn't have any research projects on cystinosis, but Dr. John Blangero – who is well known internationally for his innovative methods in statistical genetics – had a “never-been-done-before” idea that he wanted to try. He thought the Foundation's extraordinary genetic resources and expertise were well suited for an entirely new approach to studying a monogenic disease.

“With our traditional focus on complex diseases, which involve multiple genes and environmental factors, we tend to look at problems globally,” says Dr. Blangero. “Besides that, SFBR is one of the few places in the world that has the combination of state-of-the-art molecular technologies for high-throughput genetic sequencing and analysis of genetic expression, along with overwhelming computing resources [in the AT&T Genomics Computing Center] for the analysis of massive amounts of data.

“With this in mind, we decided to turn this problem on its head and ask, ‘What could we do with our genetic approaches and resources that would inform us about the [biological] causal pathway of cystinosis?’ In other words, we wanted to learn more about the biology of this disease and how the *CTNS* gene actually functions – since there is very little science on this – as well as what other genes ‘upstream’ impact *CTNS*, what other genes *CTNS* impacts ‘downstream’, and what other genes might perform parallel, or similar, functions to *CTNS* so that we could look for new drug targets and other areas of disease intervention,” he explains.

“We believe the findings from this type of study could relate not only to cystinosis, but also to other diseases, including those

caused by a similar toxic build-up of amino acids, such as Alzheimer's and Parkinson's. And if this research method proves effective in the study of cystinosis, it could become the new paradigm for the study of other monogenic, or single-gene, disorders,” Dr. Blangero says.

A series of meetings was set up with the Azars, Shepperds, and SFBR representatives. Dr. Blangero learned more about the family's plight, and they listened to his novel research proposal, which also involved a stellar molecular genetics group that had recently moved to SFBR from Australia, led by Drs. Eric Moses and John Blangero.

“As we listened to his plan, I was amazed that my children could be the impetus for something with so much potential to help other families affected by cystinosis as well as millions of people around the world who suffer from other devastating disorders,” Kim Shepperd says. “Suddenly, everything fell into place, and I knew this was a blessing.”

“Dr. Blangero and the other scientists were thinking outside the box and looking at the big picture,” says Richard Azar. “I liked that. We all did. So we said, ‘Let's do this.’”

The Azars provided an initial \$1 million gift for the creation of a new cystinosis research program at SFBR, and they have since helped the program maintain its momentum with supplemental philanthropic grants totaling more than \$700,000. Their financial support has been augmented by the generous contributions of others, including the Elizabeth Huth Coates Charitable Foundation; the Cystinosis Research Foundation – Natalie's Wish; the Southwest Foundation Forum; and numerous relatives and friends who have made individual gifts.

In two short years, SFBR investigators have embarked on several “firsts” in cystinosis research, and their results are generating excitement among not only the Azars and Shepperds but also affected families and cystinosis researchers throughout the United States and overseas.

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A new approach to single-gene disorders

One of their first steps was to learn more about the normal function and variation of the *CTNS* gene in a random, unaffected population so they could learn more about what the gene does in a healthy individual. That would lend insight into what goes wrong when the gene is disrupted.

This research approach had never been applied to the study of a monogenic disorder, nor had it been used in such a large-scale analysis. In what Dr. Blangero describes as “the single largest transcriptional profiling project ever undertaken,” the SFBR team performed genome-wide transcriptional scans on 1,240 members of SFBR’s San Antonio Family Heart Study.

What does that mean? In short, genes work by producing transcripts, or messenger RNAs, which then are turned into proteins that have particular biological effects. So the SFBR team performed genetic tests to measure the mRNA output level of all the genes in the genome of each individual studied.

At the same time, they sequenced every piece of DNA in the *CTNS* gene of 200 individuals and found the normal, common variations in the gene among individuals. “In other words, we found variations in the DNA sequence of that gene that have big effects on its output,” says Dr. Blangero.

Large-scale study produces large-scale results

Then they analyzed this massive amount of data and found more than 2,000 genes that correlate with *CTNS*,

making them the subject of follow-up studies to see if they might be good targets for disease intervention.

Some of those appear to be genes that are “downstream,” or genes that are affected by the output of *CTNS*. Researchers say these could potentially be good targets for treating disease symptoms or complications.

“In an individual who has a severely disrupted or a deleted *CTNS* gene, we might not be able to restore the function of the gene, but if we can identify genes downstream that are close to the pathology, genes that contribute to these undesirable disease outcomes, they might make good targets for drug intervention,” says Dr. Moses.

Other genes of interest are believed to be “upstream” from *CTNS*, meaning they seem to impact its function. Dr. Blangero explains, “In 60 to 70 percent of cystinosis cases, the [*CTNS*] gene is knocked out, or completely disrupted, but in other cases the disruption is more minor. So the gene is still functioning, just not to the level that it should. For that subset of cases, these genes upstream in the biological pathway might be used to help regulate *CTNS* and improve its function.”

Dr. Moses says the research team is following up on one such gene that strongly correlates with *CTNS* and that other research has shown to play a role in “cleaning out” damaging chemicals from cells. That could make it a target in fighting multiple diseases.

Other identified genes, the researchers say, appear to perform similar, or parallel functions, to *CTNS*. They’re following up on one in particular after interest was sparked from an unlikely source: yeast.

Researchers at another institution found that when the yeast equivalent of *CTNS* was “knocked out,” another



The SFBR cystinosis research team includes (counter-clockwise beginning at bottom right) Drs. John Blangero, Eric Moses, Matthew Johnson, Katy Freed and Joanne Curran.



The 'meeting of the minds' of Drs. Eric Moses and John Blangero has yielded major results in cystinosis research and a new paradigm for the study of single-gene disorders.

gene essentially “stepped up” and performed a similar function. With this exciting information, Drs. Blangero and Moses used the human genome sequence and the genome transcriptional profiles they had developed and identified one matching human gene, or homologue, to this newly identified yeast gene.

“That’s one of the things that we’re working on right now,” says Dr. Blangero. “We want to see what this gene does and if we can manipulate it. There is a big evolutionary distance between yeast and humans, so all the gene’s functions might not be preserved crossing from one to the other, but we want to see if we can manipulate this gene in such a way that it will take the place of *CTNS* in people with cystinosis.”

Pursuing hot leads

For follow-up studies on this promising homologue, as well as some of the other genes they’ve identified to be of greatest interest, SFBR researchers are now embarking on some new collaborations and methods of research.

One developing collaboration is with French nephrologist Dr. Corinne Antignac, who first discovered the *CTNS* gene. In her research at *Hôpital Necker-Enfants Malades*, a children’s hospital in Paris, Dr. Antignac has developed a mouse model in which the *CTNS* gene has been knocked out. Investigations with this model can help study the relationship of *CTNS* and the yeast homologue and other genes of interest to researchers, reveal more about these genes’ functions, and help show if and how those functions change when *CTNS* is disrupted.

SFBR researchers also are getting some help from the Cystinosis Research Network, an advocacy group that promotes awareness of and research on cystinosis and

provides support to affected families. The group hosted an international conference in San Antonio in July 2007, and SFBR researchers used the opportunity to recruit 150 members of affected families to donate blood samples for further study.

The researchers are now using these 150 samples – obtained from children with cystinosis as well as from their parents and siblings – to develop “immortalized cell lines” for a variety of complementary research projects. A pilot study grant funded by the Southwest Foundation Forum was recently awarded to Dr. Katy Freed for this purpose.

“We’ll sequence these individuals’ *CTNS* genes, and we will perform genome-wide expression profiling with each individual for comparison studies with our unaffected population,” says Dr. Moses. “From this, we’ll be able to learn more about all the different variations of *CTNS* and how they correlate with varying degrees of severity of cystinosis. We will also learn more about the effect of these mutations on the genes downstream in the biological pathway.

“And really exciting is that we’ll be able to conduct a variety of tests in these cell lines to see how we might manipulate genes upstream, downstream and parallel to *CTNS*, and how those genetic manipulations impact cystine metabolism, or the cells’ ability to clear out excess cystine. For example, we can flood a cell with high levels of cystine, then do something to over-express one of these *CTNS* correlates and see what effect it has. Is the gene we have our eye on truly a good drug target or not?”

Relishing the potential

Researchers are enthusiastic about the opportunities for discovery. “We have so many leads to explore, so many opportunities to make a significant contribution to the fight against cystinosis,” says Dr. Moses. “And we truly believe our novel research methodology will be the new paradigm for the study of single-gene disorders. It could revolutionize this field of research.”

Dr. Blangero expresses his gratitude to the Azar family for putting forth the funding to make this cutting-edge research possible, and he thanks the Shepperds for their inspiration. “When we come up with these research findings, we get the glory, but the true heroes are John Ben and Ava Shepperd and other children living with this disease. When you see what they go through on a daily basis, you see that they and their parents are true models of courage.”

As for the Shepperds and the Azars, they’re thrilled by the possibilities ahead. “It’s amazing to think that we could be part of something that could potentially help thousands of people affected by cystinosis and millions affected by other heartbreaking diseases,” says Kim Shepperd. “We’re so grateful to Foundation scientists for taking on this project and putting their hearts and souls into it. And we’re so grateful to all the donors who have contributed to this and other SFBR projects. We’re living examples that when you support SFBR, you’re truly making a difference in people’s lives.”

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Kim Shepperd holds up the completed sets of one day's medication for each of her children.

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MedDay transforms depressing chore into uplifting experience

Kim Shepperd gets a big smile on her face when she talks about her “syringe sisters,” a group of friends who have organized and volunteer for what they call “MedDay” at her home once every three weeks. The event has turned what once was an all-day, depressing task for Kim into a fun-filled and inspiring two-hour activity with friends.



For the treatment of cystinosis and its complications – as well as to help offset the side effects of some of those treatments – her children, John Ben and Ava, must take several medications every six hours, including some that taste like sulfur. To make this regimen easier for the children, Kim and her husband, John, give them their medications through syringes that fit into gastro-intestinal tubes that have been surgically inserted in the children's stomachs. The monumental task of “pulling” the large number of doses of liquid medications into syringes, especially when coupled with the additional task of mixing water with medications that come only in capsule form, was at first overwhelming.

That changed when friends Hillary Conrey and Melissa Morgan started arranging MedDay, recruiting volunteers to be part of an efficient assembly line that quickly prepares, “pulls” and organizes all the proper doses of medication needed for each child each day for three weeks. One person offers to provide lunch for all the volunteers, who take their turn at their designated workstation, grab a bite to eat, and enjoy catching up on all the latest gossip in between. When they're finished, they even clean up their own mess! It's the kind of day that puts a smile on everyone's face.



Friends work to prepare the proper doses of medication for John Ben and Ava Shepperd.

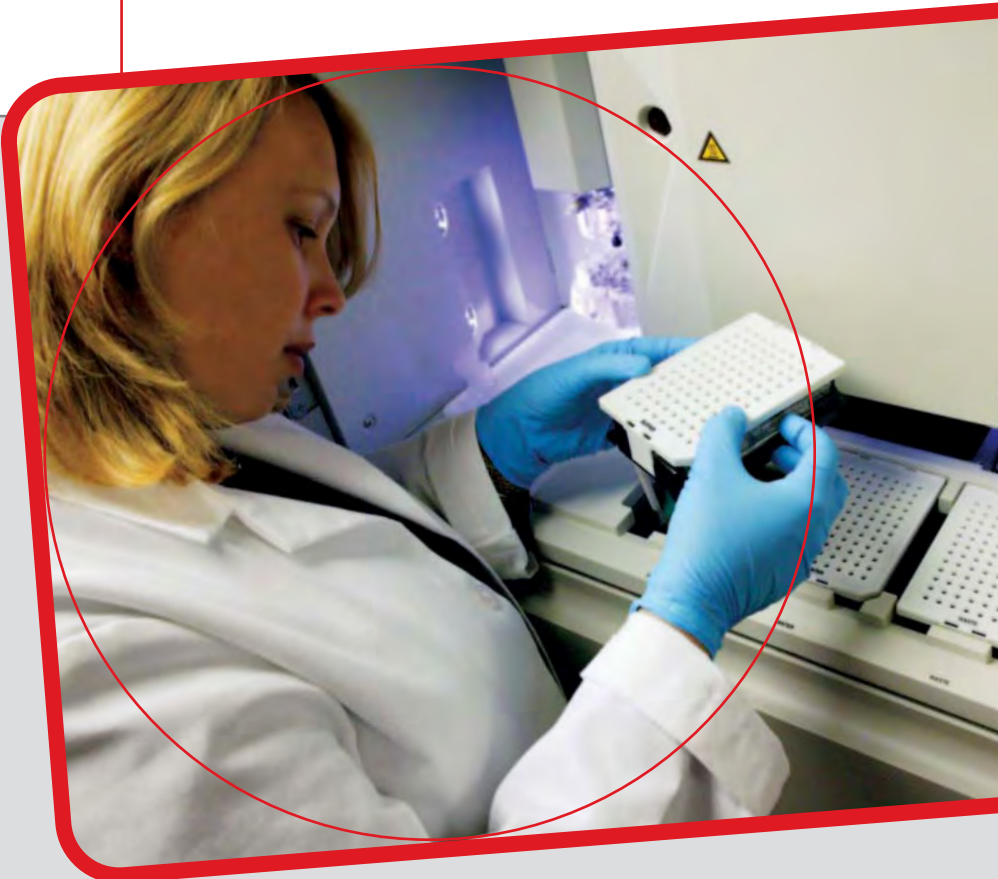


Breaking news

A separate story beginning on page 13 of this issue describes how SFBR scientists used a new discovery method to find a novel gene, called *VNN1*, that regulates levels of HDL, the “good” cholesterol. That development was possible in part because of the cystinosis research program, since it utilized a large set of human genetic profiles originally developed for the cystinosis project. Now, serendipitously, the *VNN1* discovery could lead to an exciting breakthrough in the treatment of cystinosis and many other diseases.

VNN1 is known to produce cysteamine, which helps transport excess cystine out of cells and prevents it from accumulating to toxic levels. Cysteamine also removes other dangerous things from cells, including excess glutamine, which can lead to Huntington’s and Alzheimer’s diseases, and general oxidative stress, which plays a key role in heart disease.

The new findings about *VNN1* by SFBR scientists are expected to give pharmaceutical companies good reason to pursue drugs that could increase the gene’s activity, stimulating it to produce more cysteamine naturally. That could result in new preventions and treatments for a variety of disorders, and it could reduce the need for cystinosis patients to take cysteamine orally. Then they could say “goodbye” to the drug’s terrible side effects.



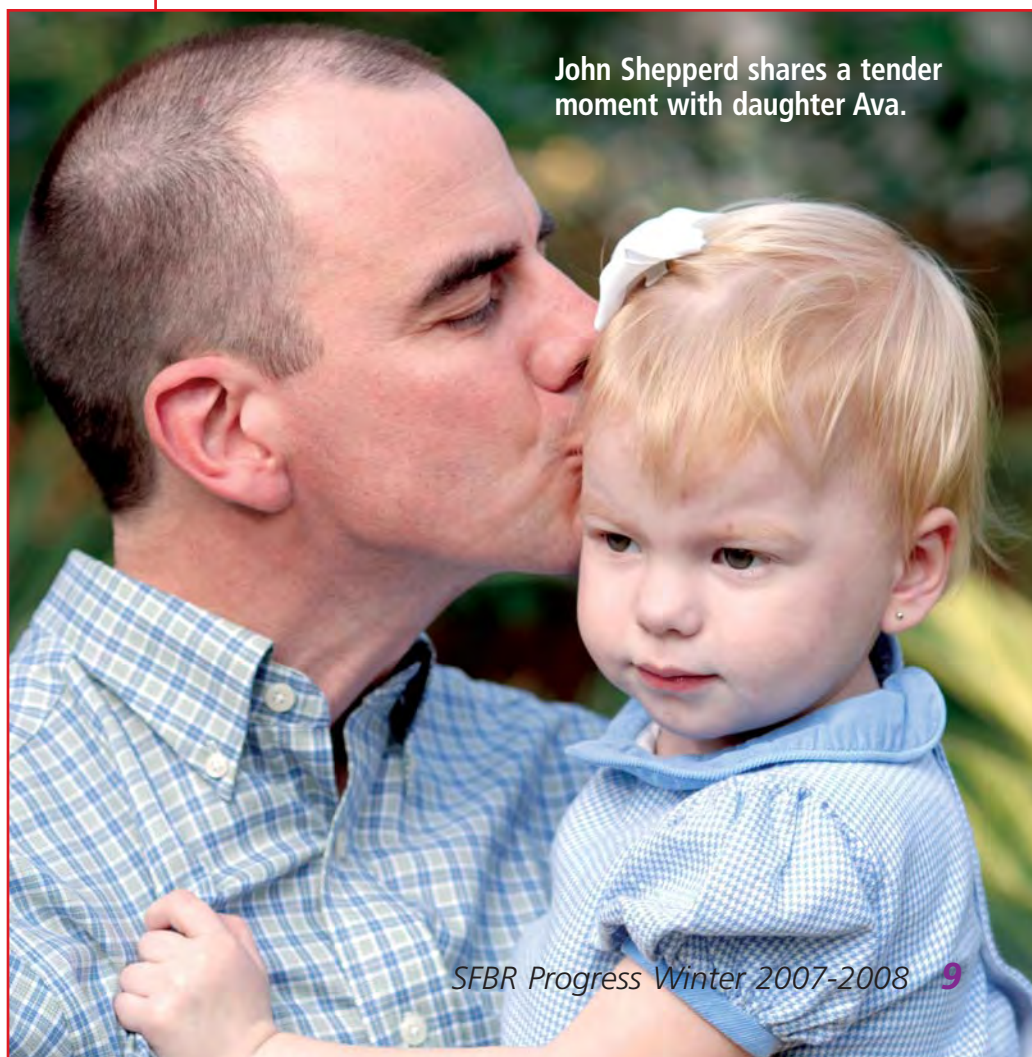
Dr. Joanne Curran and other SFBR scientists involved in cystinosis research and the discovery of the *VNN1* gene’s role in cholesterol are thrilled that each project has benefited the other.

Everyone’s invited to the Hoedown!

A few years ago, in support of their friends Kim and John Shepperd, Hillary and Chad Conrey conceived the idea for and began organizing an annual “Hoedown” as a fun way to increase awareness about cystinosis and support families living with the disease. Held at Anhalt Dance Hall – located northwest of San Antonio off of Highway 46 – the event offers information about cystinosis in a lively, family atmosphere. Participants can enjoy live music, a variety of children’s activities, plentiful food, and a children’s art auction.

Event proceeds are placed in a scholarship fund that enables affected families to attend cystinosis conferences that provide the latest information on the disease and its management, as well as a vital support network.

The next Hoedown is scheduled Saturday, April 12, from 1:00 p.m. to 6:00 p.m. For more information on the event, to purchase tickets in advance, or to volunteer to help, call 210-325-8200 or 210-275-5508.



John Shepperd shares a tender moment with daughter Ava.



SFBR at the forefront of national biodefense efforts

Department of Homeland Security funds \$1.5 million research contract to study Marburg virus

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an important part of the federal government's efforts to better characterize the threat posed by certain viruses, the Department of Homeland Security (DHS) has awarded a \$1.5 million contract to fund one of the most comprehensive research programs to date on the Marburg

virus, a hemorrhagic fever virus.

The 18-month contract with Southwest Foundation for Biomedical Research is aimed at exploring how the Marburg virus causes disease. This will include studying the progression of infection and its effect on the immune system, as well as identifying viral genetic factors responsible for disease. The goals of this project are to prioritize threats and to develop new information that will inform the development of effective treatments and vaccines through Project BioShield. Project BioShield is a Department of Health and Human Services project intended to accelerate the process of research, development, purchase, and availability of effective countermeasures against selected biological agents.

Research at SFBR on behalf of DHS' National Biodefense Analysis and Countermeasures Center will include genetic analyses of various Marburg virus strains as well as a detailed examination of the role viral and host proteins play, a field of study known as proteomics.

"Right now, very little is known about how the Marburg virus works, what causes its pathogenicity, or what accounts for the difference in severity among the seven different variants of the virus," said Dr. Jean Patterson, chairman of the Virology and Immunology Department at SFBR and the lead investigator on the contract. "These are things we need to understand in order to develop effective remedies."

"For example, previously known variants of the Marburg virus have a 40 to 60 percent mortality rate, while the Angola variant has a 90 percent mortality rate," said Dr. Ricardo Carrion Jr. of SFBR, a co-investigator on the contract. "There is little difference in the proteins among these variants, so the reason for the difference in their severity is unclear. That is one of the things we'll try to find out as part of our research."

SFBR's biosafety level 4 laboratory and its Southwest National Primate Research Center both will play key roles in the Marburg research program.

Other resources and expertise will be brought to the program by various subcontractors, including Dr. Richard Drake, director of the Scientific Center for Biodefense at Eastern Virginia Medical School, who will work with protein samples for the proteomic analysis; and INCOGEN, Inc., an informatics company that will provide data management and analysis support for the project.

"This is an exciting opportunity to continue our collaborative efforts with Southwest Foundation for Biomedical Research and Eastern Virginia Medical School,"

Dr. Jean Patterson monitors work inside the BSL-4 laboratory at SFBR.



said INCOGEN's CEO, Dr. Maciek Sasinowski. "The data generated during this project has significant potential to improve our understanding of Marburg and other hemorrhagic fevers and to develop measures against natural or deliberate outbreaks of these diseases."

"The virus transmits easily from person to person, so it is important for us to be out in front on research that could help in the development of vaccines and drug therapies," said Dr. Patterson, who also leads investigations on potential treatments and vaccines for anthrax and other biological agents.

Scientists initially identified the Marburg virus in 1967 after laboratory workers in Marburg, Germany, were infected, then others contracted the disease in Frankfurt, Germany, and Belgrade, Yugoslavia. All of those infected had handled blood, tissue, or cell cultures of African green monkeys from Uganda that had been naturally infected with the then-unknown virus.

It is endemic to Africa, where natural outbreaks typically occur every five or six years, Patterson explained. She said the virus also is a serious threat to the great apes and other nonhuman primates on the continent.

"We're excited by the opportunity to begin such a large-scale research program on the virus," she said. "As we learn more about Marburg and how it works, we'll be better equipped to help defeat it."

New animal model developed for Lassa fever research

SFBR scientists have developed a new tool in the battle against a potential biological weapon, Lassa fever, which kills several thousand people each year and leaves thousands more with disabilities such as deafness and liver damage.

In an article in the June 2007 issue of the *Journal of Virology*, Drs. Jean Patterson and Ricardo Carrion Jr. and colleagues detailed the development of a new animal model, the marmoset monkey, for use in Lassa fever research.

The marmoset is a small primate that weighs about one pound when fully grown, but it has many genetic and physiological similarities to humans. An advantage of using marmosets is that the animal's response to Lassa infection completely mimics the response found in people who develop symptoms.

The availability of the marmoset for this research is expected to speed the testing of potential vaccines against Lassa fever, including a number of candidate vaccines that already have been developed and are waiting on a model like this for testing, said Dr. Patterson, who chairs the Department of Virology and Immunology at SFBR.

Lassa fever is a viral illness that occurs in West Africa, spread by the multimammate rat. The virus is seen as a potential bioterror weapon because one of the ways that people become infected is via airborne particles contaminated with rodent excretions, known as aerosol or airborne transmission. Only about 20 percent of people infected with Lassa develop severe symptoms. Of those who get sick, the mortality rate is from 15-20 percent, but the mortality rate rises to 60 percent for those who are pregnant.



Scientists show progress with hepatitis C vaccine

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he vaccine we have today for hepatitis B was tested for efficacy and safety at Southwest Foundation for Biomedical Research. Now SFBR scientists are working with the National Institutes of Health to help find a vaccine and better drug therapies for hepatitis C, the most common cause of liver disease and liver

transplantation in the United States.

Tests by Dr. Krishna Murthy at SFBR have shown great promise with one candidate vaccine in particular. Dr. T. Jake Liang with the National Institute of Diabetes and Digestive and Kidney Diseases, along with other collaborators, has developed an experimental hepatitis C vaccine that uses non-infectious pieces of the virus to induce immunity.

In tests with chimpanzees, Dr. Murthy showed the vaccine to be protective. Of the four chimpanzees given a four-dose regimen of the vaccine, one developed a mild infection that it quickly cleared. The other three showed signs of a slightly higher level of infection, but they also cleared the virus within 10 weeks. Four other chimpanzees that had not received the vaccine all contracted chronic infections when challenged with hepatitis C.

Chimpanzees are the only species besides humans that are susceptible to hepatitis C infection. Unlike humans, however, they can carry chronic infections without ever developing liver disease. These characteristics make them ideal for vaccine studies.

Drs. Liang, Murthy and their collaborators are enthused by their initial findings, which they recently published in the *Proceedings of the National Academy of Sciences of the United States of America*. "You want to prevent the chronic infection in disease. This is the goal we are targeting, and preliminary data suggests that this is possible," Dr. Liang told the *San Antonio Express-News*.

This is good news in the battle against a disease that affects an estimated 170 million people worldwide and is dubbed "the silent epidemic." Individuals can unknowingly carry a hepatitis C infection for years, because they do not experience any symptoms until the infection eventually leads to cirrhosis, liver cancer or liver failure.

"I think we're headed in the right direction [with this vaccine]," Dr. Murthy said in an interview with KENS-TV.



In tests with SFBR chimpanzees, Dr. Krishna Murthy has shown that a candidate vaccine for hepatitis C holds a great deal of promise.



"Now we need to modify it a little bit and fine tune it in hopes that we can completely prevent infection."

In addition, he said that there are six major genetic subtypes of hepatitis C, and the vaccine has only been tested against one. So future work also will include tests with the other subtypes. Dr. Liang expects human trials with the vaccine to be at least a year or two away.

New method speeds up the search for genes related to human diseases, identifies 'good cholesterol' gene



Scientists will be able to pinpoint genetic causes of human diseases faster than ever thanks to a powerful new discovery method unveiled by the Southwest Foundation for Biomedical Research and an international team of researchers.

In the Sept. 16 online edition of the prestigious journal *Nature Genetics*, the team described its method for isolating genes that are self-regulated – meaning they harbor variations that affect

their own output – then rapidly narrowing in on genes that likely have a causal effect on a particular disease or disease trait. That approach makes it possible in many studies for researchers to quickly sift through the 25,000 genes in the human genome and see which ones should be the focus of follow-up investigations.

As proof of concept, the group recounted how it used this method to identify a gene – *VNN1* – that regulates HDL, the “good” cholesterol, a finding with major implications for heart disease.

“We basically just zeroed in on the low-hanging fruit,” said Dr. John Blangero of SFBR, who directed the study. “Instead of looking at all of the genes, we focused on the ones that strongly control their own outputs, and of those genes we then looked at the ones that correlate with disease risks. This approach narrows down the field of genes to target very quickly. While this has been done before on a very limited scale, the sheer power of our AT&T Genomics Computing Center, plus multiple generations of genetic data we have accumulated in the San Antonio Family Heart Study, allowed us to apply this method to a much larger number of study samples. No one has ever applied this method on an epidemiological scale before.”

► Continued on page 14

Home to the world's largest parallel computing cluster dedicated to human genetic research, SFBR's AT&T Genomics Computing Center allows the Foundation's scientists to analyze vast amounts of complex genetic data at record speed.

The researchers already are following up with analyses of 60 other genes that appear related to HDL cholesterol, and they are applying the method toward gene discovery for other factors related to heart disease, as well as diabetes, obesity, and cystinosis, a rare genetic disorder. They so far have found approximately 100 genes that appear related to diabetes.

"Although in this paper we show how we used the method to find a gene with a big influence on HDL cholesterol, we've begun applying this same approach to every disease that we work on and have obtained outstanding results," said Dr. Harald Göring, the SFBR geneticist who was the lead author on the paper. "It's the biggest speed-up in discovery that we've ever experienced."

Genes that exhibit major control of their own outputs are known as "*cis*-regulated" genes. The output of these self-regulated genes is primarily affected by DNA variations within the genes themselves. This means that, if a *cis*-regulated gene is found to be correlated with a disease trait, there is a greater likelihood of quickly identifying genetic variations that play a causative role.

"This paper represents a proof of principle for a rapid approach to discover genes directly involved in disease," Dr. Blangero said. "The ability to pinpoint the *cis*-regulated genes not only speeds up the discovery process, but means that you immediately have a good target for drugs to treat those diseases that they influence."

A powerful new method for genetic discovery

Blood samples from 1,240 participants in SFBR's ongoing San Antonio Family Heart Study provided the genetic material for the study detailed in *Nature Genetics*. That study includes approximately 1,400 members of 40 Mexican-American families in the San Antonio area, who are participating in a long-term investigation of the genetic determinants of heart disease, diabetes and obesity.

The researchers in this new investigation focused their analyses on lymphocytes (a subset of white blood cells) that had been obtained from the participants of the family study. Using newly available glass "chips" containing sensors for virtually all of the approximately 25,000 genes in the human genome, they measured the amount of messenger RNA, or mRNA, the output of genes that subsequently gets converted into the proteins that perform the genes' functions in the body.

In the next step, the researchers examined these gene expression patterns to identify the self-regulated genes, which come in slightly different forms that generate more or less messenger RNA.

"The expectation is that the more mRNA present, the more protein that will be made," Göring said.

This was done using extremely computer-intensive statistical analyses that are geared towards locating where in the human genome regulatory DNA variants are located. The investigators found several thousand genes that are likely to harbor DNA variants within themselves that determine how much mRNA and



Drs. John Blangero and Harald Göring discuss the new research method used to find the *VNN1* gene's role in HDL cholesterol. The AT&T Genomics Computing Center in which they stand played a critical role in the discovery.



Dr. Joanne Curran performed many of the molecular analyses and genetic expression profiles involved in the *VNN1* gene discovery.



ultimately protein is produced by a gene. This told them which genes were *cis*-regulated.

Finding an HDL gene

To demonstrate how genetic expression patterns can be used to speed up the search for disease-influencing genes, the researchers chose HDL cholesterol as an example. To identify those genes that influence a person's "good cholesterol" level, they statistically correlated the gene expression profiles with the variable HDL cholesterol levels in the San Antonio Family Heart Study participants.

Of the more than 60 *cis*-regulated genes they found to have some correlation, one gene clearly stood out. That gene was *VNN1*, which produces the protein vanin-1. "*VNN1* showed by far the strongest correlation with HDL cholesterol. High levels of the mRNA it produces correspond with high levels of HDL in our study participants," said Dr. Göring. "In addition, it was one of the genes that was most highly *cis*-regulated, meaning that sequence variations within the gene itself are highly likely to influence the level of production of vanin-1 and play a causative role in variation of HDL cholesterol levels among individuals."

So the logical next step for the group was to sequence the gene itself, focusing particularly on its "promoter region," the region known to be of the greatest regulatory importance in a gene. Analysis of that sequence revealed 20 variants within *VNN1*. Statistical investigations revealed that some of these influenced the gene's output and were correlated with HDL levels. Follow-up molecular studies in the laboratory showed one of those variants had a direct functional consequence on the gene's output and likely influences HDL levels.

"So we finished our study with a bit of biology to prove that the statistical associations that we saw also have direct biological validity," said Dr. Blangero.

The study was funded by ChemGenex Pharmaceuticals, based in Geelong, Victoria, Australia; the National Institutes of Health; and a philanthropic research grant from Dianne and Richard Azar of San Antonio.

Application to other health issues

"This research method has tremendous potential to accelerate the development of pharmaceutical therapies to target the genetic causes of a whole range of diseases that affect people worldwide," said Dr. Greg Collier, CEO of ChemGenex.

"This will become a standard approach in epidemiological studies because it gives you such a good overview of what the genes are doing," Dr. Blangero said. "It's an absolute gold mine for gene discovery."

In addition to Drs. Göring and Blangero, the team of SFBR investigators on this study included Drs. Joanne Curran, Matthew Johnson, Thomas Dyer, Jac Charlesworth, Shelley Cole, David Rainwater, Anthony Comuzzie, Michael Mahaney, Laura Almasy, Jean MacCluer and Eric Moses.

Along with ChemGenex, other institutions participating in the study included the Deakin University in Warrnambool, Victoria, Australia; the International Diabetes Institute of Caulfield, Victoria, Australia; the University of Western Australia in Crawley, Western Australia; and the Medical College of Wisconsin in Milwaukee.

Wave of breakthroughs on horizon thanks to SFBR donors



FBR scientists aren't simply on the cutting edge of genetic research. In many cases, they actually are the cutting edge, and that's due in large part to the partnership of SFBR benefactors.

The advances highlighted in the article "New method speeds up the search for genes related to human diseases, identifies 'good cholesterol' gene" (pages 13-15) were made possible by a mingling of federal, private and philanthropic support, with funds from the National Institutes of Health for the San Antonio Family Heart Study it built upon, funds from ChemGenex Pharmaceuticals for the genetic analyses, a philanthropic grant from Dianne and Richard Azar that paid for the transcriptional profiles utilized in the investigation, and a previous gift from the AT&T Foundation that enabled SFBR to build its AT&T Genomics Computing Center, which was critical for the massive statistical analyses conducted as part of the study.

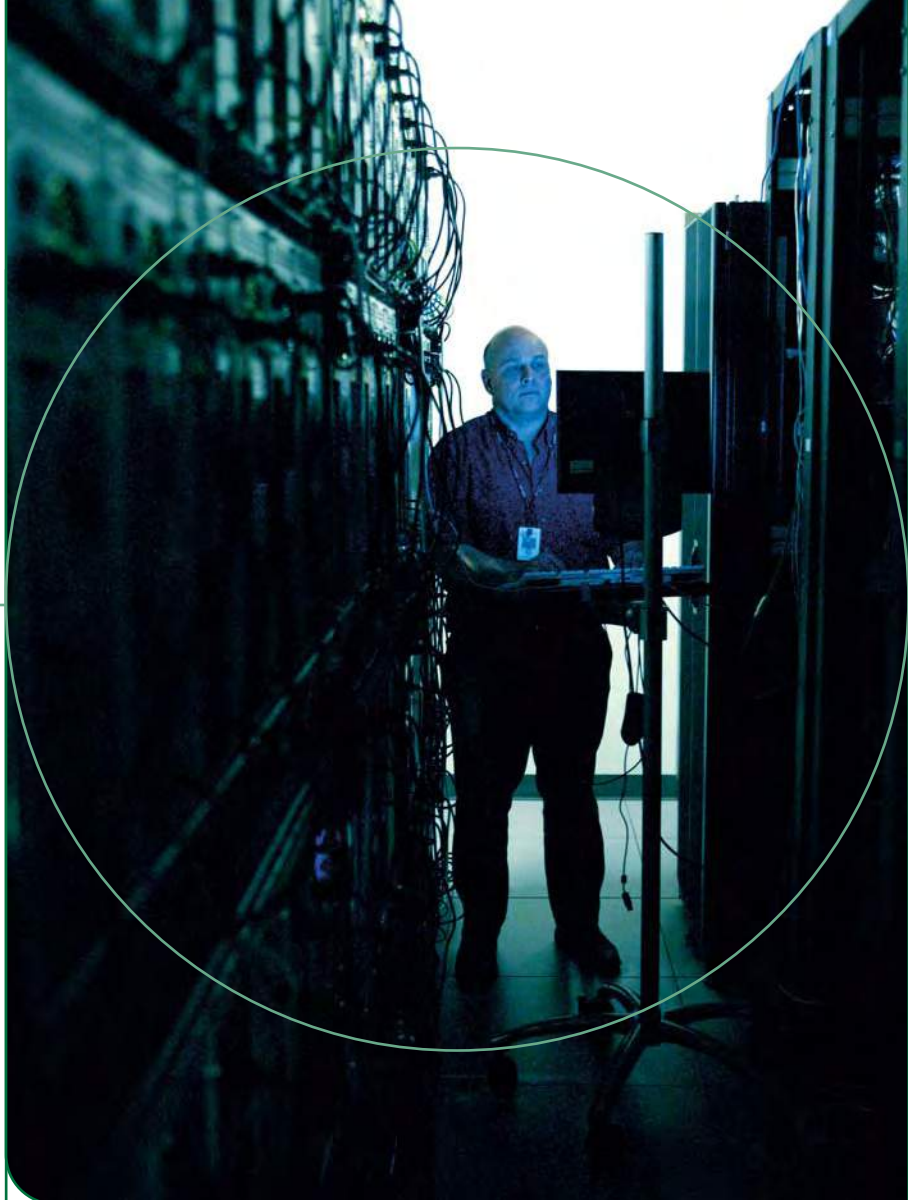
Now donors have paved the way for the next wave of cutting-edge research that is set to follow.

AT&T Foundation doubles SFBR computing power

A new \$1 million gift from the AT&T Foundation, the charitable philanthropy organization of AT&T, Inc. (NYSE: T), has allowed SFBR's AT&T Genomics Computing Center to double the power and speed of its "computer ranch," the world's largest parallel computing cluster dedicated to human genetic research. The gift funded an update in the center's networking system, improvements in power supply, and the purchase of 375 new four-processor Opteron-based computers, allowing the center's "computer ranch" to expand from 1,500 processors working in parallel to a total of 3,000.

"This leap in computing power makes our facility more than 2.5 times the size of that of any of our competitors around the globe and guarantees the primacy of SFBR as the world's leading center for the genetic analysis of common complex diseases," said Dr. John Blangero, the center's director.

The expansion of the computer ranch in 2003 after the construction of the AT&T Genomics Computing Center

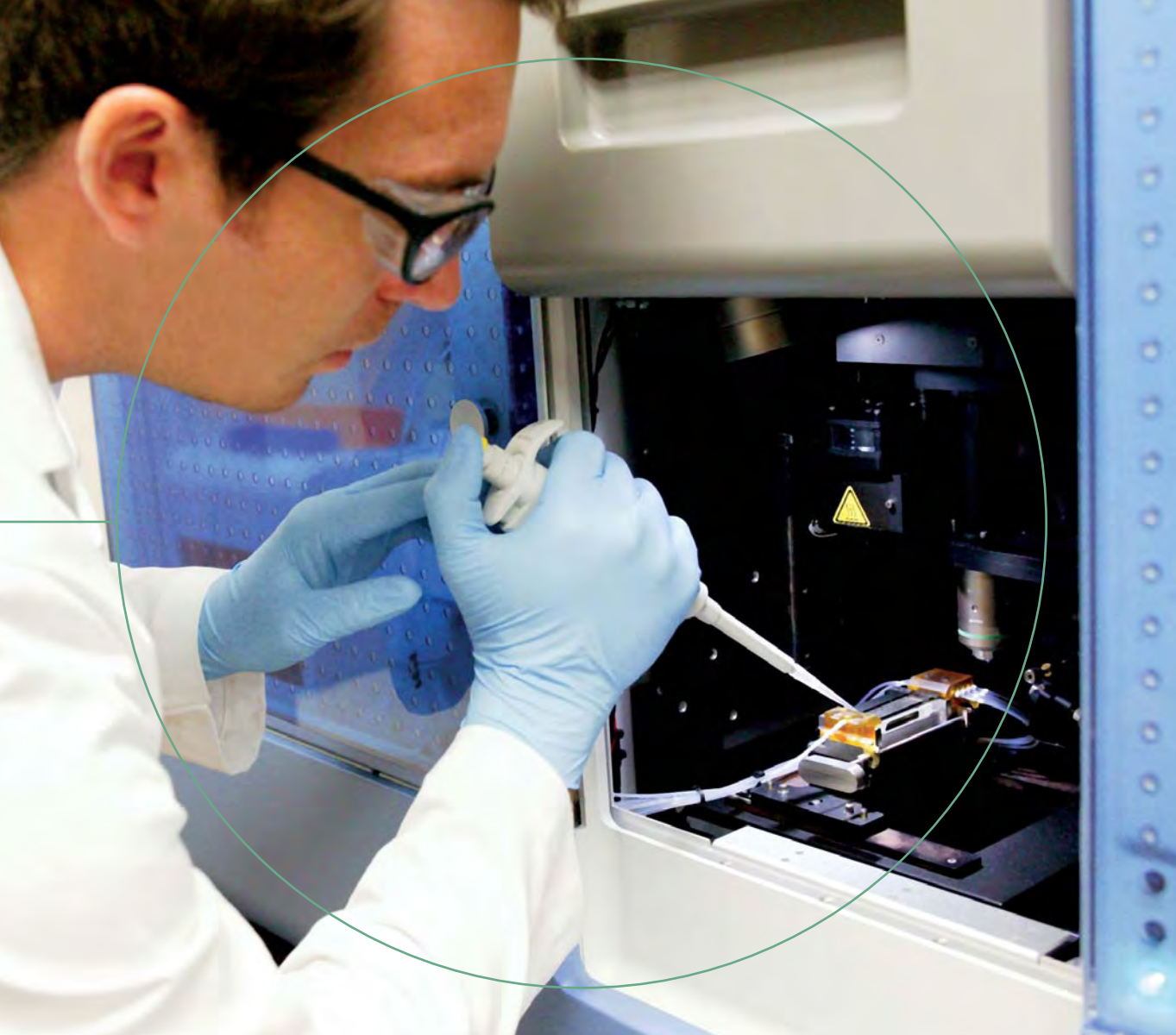


allowed SFBR geneticists to put their novel statistical methods and genetic software to greater use, completing in a matter of minutes complex genetic analyses that once took months. That has enabled numerous breakthroughs, including the identification of the locations of genes that play a role in heart disease, diabetes, osteoporosis, inflammation and parasitic diseases. Dr. Blangero expects the current upgrades to make a similarly dramatic impact, especially when coupled with other gifts to the Foundation's laboratory capabilities.

Coates Foundation donates state-of-the-art sequencer

A \$300,000 gift from the Elizabeth Huth Coates Charitable Foundation has funded the purchase of next-generation genome sequencing technology, the Illumina Genome Analyzer. This new piece of genetic laboratory equipment gives SFBR researchers the ability to produce genetic data at an unprecedented rate.

With sequence output that is 1,000 times greater than genetic sequencers used for the Human Genome Project, this machine can complete in one week a similar amount of DNA sequencing work that took all of the facilities involved in the Human Genome Project over six months to achieve, said Dr. Sarah Williams-Blangero, chair of the SFBR Genetics Department. "The decrease in time required to conduct genetic sequencing [of study samples] will allow SFBR scientists to undertake much larger investigations and examine much broader stretches of DNA than previously thought possible," she said.



Far left: Richard Polich works in the newly upgraded AT&T Genomics Computing Center, which houses the world's largest computing cluster for human genetic research. At left: Dr. Matthew Johnson makes use of a new genetic sequencer purchased with funds from the Coates Foundation. Together, these donor-sponsored enhancements to SFBR resources are allowing scientists to catch the next great wave of genetic research: whole genome sequencing studies.

Unleashing the potential of the human genome

Dr. Williams-Blangero explained that the combined advances in genetic sequencing and computing technology are propelling SFBR geneticists to the future of genetic research: whole or nearly whole genome sequencing studies. In these kinds of investigations, scientists shift their approach from the traditional method of focusing on the examination of one gene at a time to examining all, or a large subset of, the approximately 25,000 genes in the human genome simultaneously.

"This is a revolutionary new approach that will dramatically enhance all of our ongoing genetic studies," said Dr. Williams-Blangero.

For example, in the case of the cystinosis research described in a separate article in this publication, SFBR scientists have identified over 1,000 genes whose activities appear to be correlated with that of the gene known to be defective in individuals with the disorder. Now, instead of trying to look at each of these genes individually and trying to piece together how each fits into a complicated puzzle, researchers can sequence the whole genome, or a large stretch of it, and look at all 1,000 genes at once.


"That will allow us to further pinpoint the potential causal pathway that the disease takes when it leads to damaging symptoms associated with pathology," said Dr. John Blangero. "And by rapidly identify these genetic players, we can generate subsets of potential genes that may be useful as drug targets to relieve or even eliminate symptoms of the disease."

Scientists also can use whole genome sequences and the powerful analytical force of the AT&T Genomics Computing Center to identify disease-related genes that might have been missed with previous, more limited research techniques.

"In the past, we've had to do things to help us prioritize and choose a single gene or a small subset of genes to examine. But what if we made a mistake in our prioritization and missed the most important gene in the process we're studying?" asked Dr. Blangero. "Now we won't have to worry about that, because we can look at all the pieces in the puzzle at once and see how they fit together as a whole. Then, when we find the genes we're looking for, we'll be able to go right back to the sequence and see what particular variants within the DNA of those genes are causing their effect. We'll have everything we need in our hands at one time. This will speed up discovery dramatically."

In the end, the whole genome studies and the transcriptional profiles funded by the Azars are expected to complement one another. "We can lay these two tools side by side and learn more about one from the other, because each tells us something different about what the genes are doing and how they work."

Dr. Williams-Blangero said she is eager to see the payoff of applying these resources to SFBR's 16 human genetic research projects that involve more than 20,000 study volunteers. The projects are aimed at advances in preventing and treating heart disease, diabetes, obesity, osteoporosis, malaria and helminthic (worm) infections. With the addition of these new research resources, she expects to see the Foundation also undertake new ventures in the field of cancer genetics.



Baboon study sheds light on role of vitamin E in heart disease prevention



onflicting reports about the potential benefits of dietary supplements can make a person's head spin. That's certainly been the case with vitamin E. Some human studies have shown this antioxidant to play a protective role in cardiovascular disease, while other studies have shown it to have no effect at all. So the question on many consumers' minds is, "Should I increase my vitamin E intake or not?"

Scientists at Southwest Foundation for Biomedical Research do not have a definitive answer to that question yet, but their research with baboons has shed light on why human studies have been contradictory and why the answer isn't as clear cut as one would hope. In fact, the answer might be "yes" to one individual and "no" to another.

In the September issue of *The American Journal of Clinical Nutrition*, SFBR scientists explain their findings from a study with 250 baboons on a diet with equal levels of dietary fat and cholesterol but varying degrees of vitamin E concentration.

"What we found was that vitamin E had a significant effect on cardiovascular disease risk factors, but those effects went in opposite directions. Some of the effects were positive, and some were negative," said Dr. David Rainwater, the paper's lead author. "This leads us to believe that the discrepancies in human studies are due to which effect is emphasized in the group of people studied."

Dr. Rainwater explained that the baboons that consumed higher levels of vitamin E had lower levels of oxidized LDL cholesterol. "Oxidized LDL is believed to be a major player in terms of promoting atherosclerosis (the build up of fatty plaques in the arteries) and in cardiovascular disease in general," he said. "So in this way, vitamin E was shown to play a protective role."

However, findings about vitamin E's effect on HDL, the "good cholesterol," were contradictory. Higher levels of vitamin E in the diet increased levels of apolipoprotein A-1 (apo A-1), which helps HDL remain soluble in the blood. On the other hand, it decreased the average particle size of HDL.

"And that is a bad thing, because a decrease in the size of HDL particles is generally associated with an increase in atherosclerosis," said Dr. Rainwater. "So we found that vitamin E is exerting two different effects on HDL properties, one positive and one negative with respect to heart disease."

While the contradictory results are frustrating, the problem might not be so much with vitamin E as it is with our genes. This scientific investigation further revealed that vitamin E's positive influence on apo A-1 levels were not genetically influenced, but genes do appear to play a role in the negative effect vitamin E can have on HDL particle size.

"So although this study doesn't give us a definite answer about whether or not everyone should increase their vitamin E intake, it does help explain the reason for the controversy over dietary vitamin E and its influence on cardiovascular disease," said Dr. Rainwater. "It also tells us that vitamin E might be beneficial to some individuals and not to others depending upon their genetic makeup. That means we need to conduct further investigations to find the genes involved."

Other scientists contributing to this investigation were Drs. Michael Mahaney and John L. VandeBerg with SFBR and the Southwest National Primate Research Center; and Dr. Xing Li Wang with Baylor College of Medicine in Houston.

Research funding was provided by the National Heart, Lung and Blood Institute (NHLBI) and the National Center for Research Resources (NCRR), both part of the National Institutes of Health.

Opossum sequence is awesome for research

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he prestigious journal *Nature* recently announced the genome sequencing of the gray, short-tailed opossum, *Monodelphis domestica*, an animal originally developed as a model for scientific studies at Southwest Foundation for Biomedical Research and now utilized by researchers around the globe for a wide variety of research on human health and disease. The tiny *Monodelphis domestica* is the first marsupial to be sequenced.

SFBR Chief Scientific Officer Dr. John L. VandeBerg, who first developed the animal as a scientific model and who served as a co-author on the *Nature* article, explained that the genome sequencing is poised to have a significant impact on biomedical research.

"The *Monodelphis* has unique properties that make it particularly useful in studies of fetal development, genetic factors related to high cholesterol and melanoma [skin cancer], as well as the quest to find ways to repair injured spinal cords, among other areas of research," he said. "Having the animal's genetic sequence will accelerate the rate of research developments in all these areas."

Scientists in Cambridge, Mass., at the Broad Institute Sequencing Center of the Massachusetts Institute of Technology (MIT) and Harvard University led the multi-institutional project sponsored by the National Institute of Human Genome Research, part of the National Institutes of Health. Kerstin Linblad-Toh oversaw the project at the Broad Institute.

The opossum that was sequenced came from SFBR's fully pedigreed *Monodelphis* colony, the largest such colony in the world. SFBR also contributed to the white paper nominating the *Monodelphis domestica* as the first marsupial to have its genome sequenced.

Editor's note: Following several years of funding by the National Institutes of Health in the 1980s, strong and consistent grant support from the Robert J. Kleberg Jr. and Helen C. Kleberg Foundation has been used to sustain and enhance the Foundation's *Monodelphis* colony since 1990. The Kleberg Foundation's awards have provided for the maintenance of the colony, the continued development of genetic stocks and strains, and pilot studies to utilize this animal's unique characteristics for new, innovative research applications.



The *Monodelphis* has unique properties that make it particularly useful in studies of fetal development, genetic factors related to high cholesterol and melanoma [skin cancer] ... and the repair of injured spinal cords."

— SFBR Chief Scientific Officer Dr. John L. VandeBerg

J.R. Hurd succeeds John Kerr as chairman of SFBR



you've kept up with local news or attended SFBR-sponsored events over the past few months, you've no doubt noticed a change in the face of SFBR leadership at the Board of Trustees level. That is because, at its June 28 meeting, the board elected J.R. Hurd as its new chairman.

Hurd's election followed John Kerr's decision to step down from this volunteer leadership position after chairing the board since 1998. Kerr continues to serve as an SFBR trustee, and he remains SFBR's interim president as the board conducts a search to fill this full-time position.

"John Kerr has done a wonderful job leading the Foundation through a decade of enormous change," Hurd said upon his appointment. "When you consider how dramatically the world of science has changed and the tremendous things the Foundation has done to stay on the leading edge, you really develop an appreciation for how far we've come in a short period of time. John's constant focus on the Foundation's mission and his calm leadership in the face of challenges have been key to that progress."

He continued, "I've really enjoyed working closely with John in my role on the board. Now, as chairman, I look forward to working with him, the other trustees, and SFBR faculty and staff to further advance the Foundation's mission. I'm very passionate about that, because I believe the Foundation has the capacity to do more for mankind than anything else I could do in my life."

Hurd brings with him a great depth of professional leadership experience in addition to his strong commitment to advancing SFBR's mission of improving human health through biomedical research.

Since 1995, he has served as chief executive officer for Hurd family companies that have operated in South Texas since the 1940s, focusing on oil and gas exploration, real estate development, ranching and investments.

Prior to his leadership role in the family businesses, he led a highly successful career as an attorney with the Houston-based international law firm of Vinson & Elkins. His 24 years with the firm included a nine-year stint in London, England, where he was promoted to the position of partner in charge of the European Practice Group.

Inspired by the work of the Southwest Foundation for Biomedical Research and what he describes as "its capacity to



J.R. Hurd shows preliminary plans for a residential real estate development designed by Hurd Urban Development, one of the family companies he leads. As the new chairman of SFBR, he also has plans to help the Foundation build upon its long history of scientific success.

improve the state of all mankind," Hurd made a major commitment to SFBR in 1998, joining its Board of Trustees and accepting an appointment to the board's Executive Committee. In this leadership role, he has been substantively involved in the major undertakings of the Foundation during a period of unprecedented growth and progress.

Now as chairman, Hurd said his top priorities include attracting additional scientists with international reputations to the SFBR faculty, intensifying collaboration with local research institutions to build synergies and accelerate the pace of scientific advances, continuing development of SFBR's facilities to help scientists stay on the cutting edge, and attracting a new generation of leaders from the community to the Foundation's board to ensure that SFBR remains a driving force in biomedical research.

"It has been deeply rewarding to serve in a leadership position during a period of such exciting growth in so many of the Foundation's programs and strengths, all of which has been accomplished with the strong support of the Foundation's distinguished Board of Trustees and nationally prominent scientific faculty," Kerr said. "Now I look forward to J.R. Hurd's tenure at the helm. I've worked very closely with him during my time as chairman, and I know that he has the leadership and the determination to continue to move the Foundation forward in a dynamic fashion."



Trustee Spotlight:

J.R. Hurd

Over the summer, the Progress editor spoke at length with SFBR Chairman J.R. Hurd about his previous accomplishments, his current business enterprises, his commitment to SFBR, and his ideas for helping the institution continue on its path of success. Excerpts from that interview are shared on the following pages, as Mr. Hurd is this issue's "Trustee Spotlight."

You bring a tremendous amount of professional experience to your role as SFBR chairman, not the least of which includes 24 years as an attorney and then partner with Vinson & Elkins. How did you come to be partner in charge of the firm's European Practice Group?

That was somewhat ironic, because my real interest was in Latin America. I got my undergraduate degree in Latin American history and then was awarded a Fulbright Fellowship to study in Ecuador. So after I finished my law degree and went to work for Vinson & Elkins, I thought I would practice international law in South America. That's when the idealism of the 1960s collided with reality. The political climate of the day in Latin America was not hospitable to foreign capital, and there was no work there for international lawyers.

One fall day in 1970, my managing partner told me I was going to be a European-based lawyer. My family and I moved to London, and I worked in Europe and the Middle East. I did a lot of transactional work involving natural resources, including financing the development of North Sea oil and gas deposits and negotiating for oil and gas exploration rights all around the Middle East and West Africa.

The experience of my youth was especially beneficial, since I grew up around drilling rigs and oil and gas fields. My grandfather, O.W. Killam, was the first person to find oil south of San Antonio. He taught me the nuts and bolts of the business when I was just a little kid driving around with him. Then as a teenager, I worked for him during the summer in the South Texas oil fields in 110-degree weather. That's one of the things that prompted me to become a lawyer. I liked the fact that lawyers work in air-conditioned offices.

► Continued on page 22

Inspired by the work of the Southwest Foundation for Biomedical Research and what he describes as "its capacity to improve the state of all mankind," Hurd made a major commitment to SFBR in 1998, joining its Board of Trustees and accepting an appointment to the board's Executive Committee. In this leadership role, he has been substantively involved in the major undertakings of the Foundation during a period of unprecedented growth and progress.

Trustee Spotlight, continued from page 21

What brought you back to the United States?

While Vinson & Elkins has offices overseas, it is an American firm that seeks to give its clients the same touch and feel they would get in Houston or Washington or Dallas. So after nearly a decade in Europe, I was in danger of “going native,” you might say, and not being able to give that American feel. In fact, when my wife, Joanie, and I heard our children talk about “those Americans,” we knew it was time to come back to the United States.

Why did you leave Vinson & Elkins and assume the role of CEO for the Hurd family companies?

Actually, I remembered the days when I worked in the South Texas oilfields and thought I’d never want to come back to work for the family business. But as my father [John Hurd] got older and it became obvious he wouldn’t be able to run the operation forever, I changed my mind. I’d worked with a number of family businesses as a lawyer, and I knew the prospects for our business were not good without a family member as the CEO. So I returned, and now I’m doing exactly the same thing my grandfather did 80 years ago. He was in oil and gas, real estate development, investments and ranching.

You run a group of Hurd family companies based in San Antonio, do you not?

I’m CEO, but my sisters and I are equal partners in the business. I like to say that they’re my bosses, since there are three of them and one of me. But they’re great partners, and now our children are partners in the business as well.

Hurd Enterprises is one of our four operating businesses. We explore for oil and gas in deep South Texas and up and down the Texas Gulf Coast from Beaumont to Brownsville. Obviously, this is a heavily explored oil and gas province, but it’s still relatively under-explored at depth. By that I mean there are not that many wells that have been drilled below 12,000 feet, which is what we do a lot of the time.

What is the focus of the other Hurd companies?

Hurd Investments, as indicated by its name, focuses on financial investments. Hurd Urban Development is our real estate development company. As is the case with our oil and gas business, we try to find our niche, doing what others are not and sticking with the area we know. We rarely venture very far away from San Antonio or Laredo.

In conjunction with our affiliate, R.L. Worth & Associates, we have built or purchased a wide variety of projects. At this time, we’re concentrating on multi-tenant, multi-story, suburban office buildings in San Antonio. Our projects include the Quarry Heights building on Broadway and the new building on Loop 1604 occupied by NuStar Energy. Next to that, we’re building a twin building that will be occupied by Citibank, Keller-Williams, Stewart Title and other tenants.

You particularly enjoy running the Hurd Ranch Company. What is it you love so much about the ranching business?

Just as with any agricultural business, at the end of the day, you can’t even pretend to be able to control it. Whether or not it rains controls it. Whether the cattle perform controls it. The calendar is out of your control. You have to do certain things when the calendar dictates, and it’s a seven-day-a-week business, which I like. Fundamentally, however, I just happen to like bovines. My wife says I spend too much time around the cattle and that they all know me by name. But I love running the ranching operation on a hands-on basis. My children say that I’m never going to turn it loose, but I’m going to surprise them one day.

You seem to have another real love. You’re obviously passionate about SFBR and your involvement with it.

When I moved back to San Antonio, I took a tour of the Foundation to honor my father. He had been a trustee for a number of years and was obviously committed to the Foundation’s mission. As it turned out, that tour changed my life. It blew my mind. I couldn’t believe that, right here in San



SANTA GERTRUDIS BREEDERS INTERNATIONAL
SALES RECORD

CLASSIFIED HERD NO. 113 Sales Record No. 6697

Sold to: O.W. Killam
Address: Frio County, Texas
Date: 8-31-1954

I certify that:
(1) the above animal is out of a Certified branded cow and a Certified branded bull. If approved by an Appraiser, Consigner, this animal will be accepted by the association, or
(2) the above animal carries the association brand.

DO NOT WRITE IN THIS SPACE
I/we certify that this animal has been inspected, approved and branded: 558

J.R. Hurd has loved cattle and ranching since his childhood. Above is the bill of sale for his first bovine, purchased by his grandfather, O.W. Killam. At right, he enjoys time on his ranch in Frio County.





Antonio, there was so much scientific talent and so much capacity to change the state of all mankind. I became passionate about the Foundation very quickly, and I remain passionate about it today. Through my involvement with it, I have the chance to do more for mankind than anything else I could do with my life.

You've been an active member of the Foundation's Board of Trustees since you joined it in 1998, especially through your role on its Executive Committee.

I've been substantively involved in everything that's gone on at the board level since that time. That includes the Foundation's tremendously successful capital campaign, the mutually beneficial rearrangement of our relationship with Southwest Research Institute, and the search for a new president to succeed Dr. Frank Ledford. While that search did not turn out as we would have hoped, we learned a lot from it. As we go forward to find John Kerr's successor, we're going to benefit from that experience.

As you and John Kerr have worked together, you seem to have developed a great deal of respect for him and the leadership he's provided to SFBR.

It's really an honor to follow John as chairman. He's a great leader who has been a serene and calming influence in times of crisis, always keeping his eye on Tom Slick's vision and never getting ruffled, never losing his focus on where we needed to go and what we were about. He's steered the organization through a decade of tremendous advancement. In 1998, the Foundation was not yet designated as a National Primate Research Center by the National Institutes of Health, nor had we built our state-of-the-art virology complex and the nation's only privately owned BSL-4 laboratory. Now the primate center and the BSL-4 lab are two of our most extraordinary assets. And consider all that's happened in the world of genetics since that time and the tremendous strides our Genetics Department has made. In the midst of the scientific advances and the campus upgrades that have enabled them, the Foundation's permanent endowment, which is vital to our operations, has nearly tripled. As an organization, we should look back on the past decade and be proud of what we've achieved under John Kerr's leadership.

As proud as you are of what the Foundation has accomplished, you have some goals as chairman to build on that history of success. Would you describe some of those goals?

Let me start by saying that a board should never try to dictate where science will go. One of the keys to the Foundation's success has been our scientists' freedom to pursue their intellectual curiosity. Our job as trustees is to provide the resources, both physical and financial, the scientists need to follow their dreams and intellect. So the first thing I say is, "We'll go where science takes us." And nothing should be sacred. If we cannot be world class in an area, we ought not to be doing it. So, we will go where our scientists want to go as long as we can do it in a world-class way.



J.R. Hurd strikes a pose with a portrait of his father, John Hurd. Today, J.R. follows in his father's footsteps, both as CEO of the Hurd family companies and in his dedicated commitment to SFBR and service on its Board of Trustees.

Having said that, one of my goals is to attract additional outstanding scientists to the Foundation. We've had tremendous success "growing our own," and we will continue that. But at the same time, this is a great place to do science, and we need to recruit scientists with international reputations, the best and brightest, to strengthen our research base and enhance our intellectual capital. This is an area where our increased endowment will be particularly important.

Second, we need to expand our collaborations with other local research institutions, because that will allow all institutions to leverage all of their talents in an important way. Our scientists have built many local collaborations already, and as we expand upon and deepen those relationships, we'll create enormous synergy and increased potential for scientific advances.

Third, we need to continue to develop our physical facilities at the Foundation. Great science needs great facilities, so we need to continue our efforts to ensure that SFBR researchers are working in the best facilities possible.

Finally, I want to make sure that our Board of Trustees remains receptive to new ideas and new people and maintains its relevance to the community. As I look at our board today, I see some of San Antonio's greatest leaders, many of whom have long-time individual or family associations with the Foundation. That's part of what is special about this place. People get engaged with the Foundation, and they stay engaged for a long time. That's wonderful. We need their continued commitment, but we also need to build upon it. San Antonio has grown. There are new leaders who have come with new ideas, and we need to bring some of those individuals onto our board so that we get the benefit of their new visions.

Southwest Foundation is well on the way to becoming one of the very best independent research institutions in the country, if not the best. I feel honored and privileged to be able to play a role in helping the Foundation achieve this recognition.

Voelcker Fund gives big boost to innovative research



FBR sends a million thanks to the Max and Minnie Tomerlin Voelcker Fund – literally. Earlier this year, the Voelcker Fund provided \$1.3 million in gifts and pledges to support new and innovative pilot studies at SFBR and the operations of the Southwest National Primate Research Center's pedigreed baboon colony.

The Voelcker Fund pledged \$400,000 annually for three years to provide seed funding to allow researchers to prove research concepts and develop preliminary data necessary to support research grant requests to the National Institutes of Health.

In addition, a Voelcker Fund gift of \$100,000 will be applied to operating costs of the primate center's pedigreed baboon colony, the world's largest such colony and an unparalleled resource for research on genetic factors that influence human health and disease, including susceptibility to heart disease, diabetes, obesity, osteoporosis, and a broad spectrum of other health problems.

"This Voelcker Fund investment in pilot studies will empower our scientists to pursue their best ideas and develop research that can attract multi-million-dollar grants from organizations such as the National Institutes of Health," said SFBR President John C. Kerr. "So the return on investment is often tremendous. We applaud the Voelcker Fund for recognizing that and committing so impressively to these early-stage studies. We're also very grateful for the infusion of operating capital to help maintain our pedigreed baboon colony, a very important medical research resource."

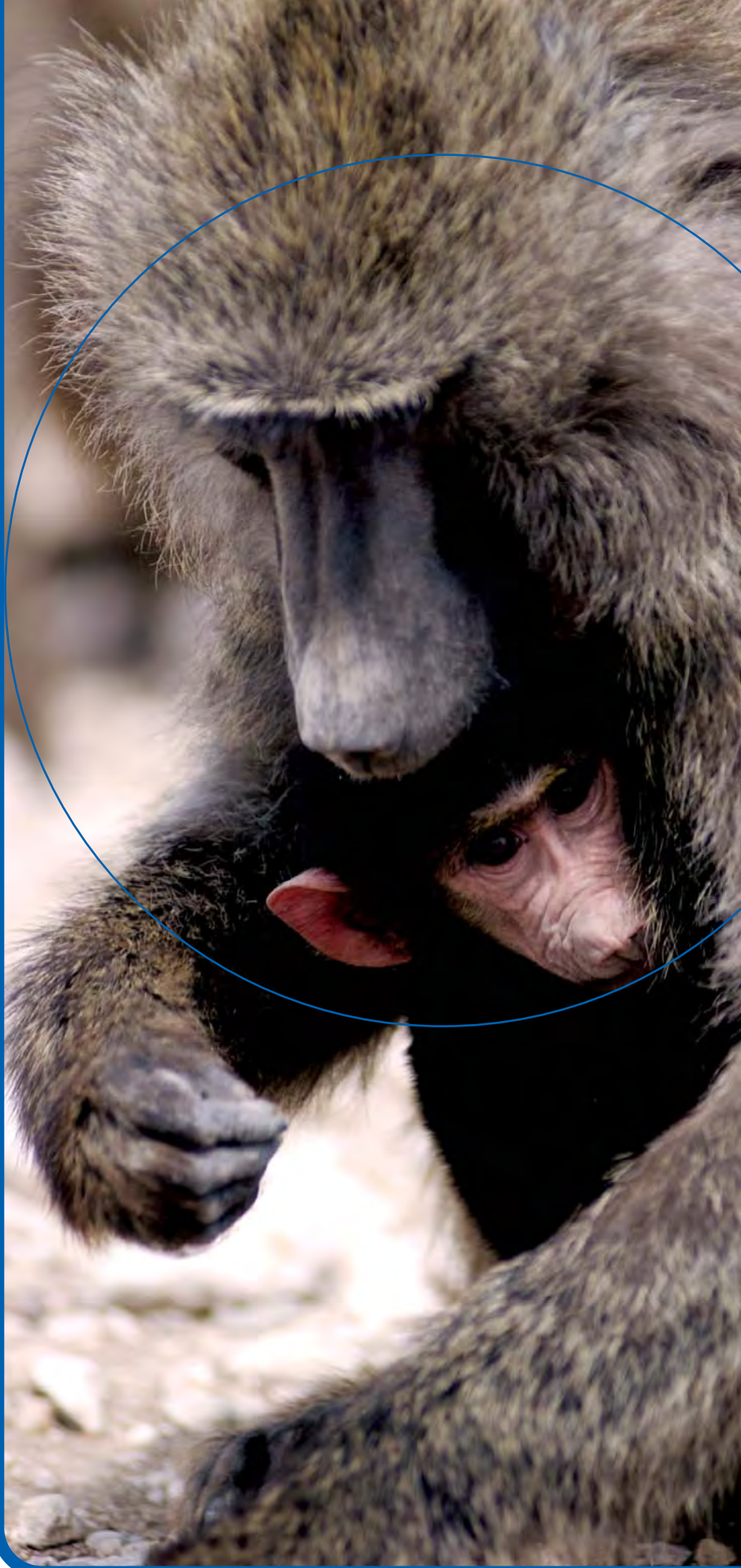
"SFBR is a premier research foundation in Texas and the United States," said Banks M. Smith, trustee of the Voelcker Fund. "The professionalism and dedication of their scientists are second to none. By supporting their pilot studies, we're confident we can leverage these funds to obtain more substantial federal research grants."

Eight new pilot studies benefit from Voelcker Fund donation

After a competitive, peer-reviewed application process completed in October, eight SFBR scientists were selected to receive pilot study grants with this year's \$400,000 donation by the Max and Minnie Tomerlin Voelcker Fund.

- Dr. Vidya Farook, along with co-investigator Dr. Sobha Puppala, will conduct a novel study on the link between

cardiovascular disease, gallbladder disease, and a common risk factor for both: elevated levels in the blood of an amino acid known as homocysteine. Specifically, the team will begin investigations with a Mexican American population to uncover common genetic influences on these conditions, with the ultimate aim of facilitating the development of new preventions, diagnostics and treatments for cardiovascular and gallbladder disease.





- Drs. John Blangero, Joanne Curran and Melanie Carless will use state-of-the-art genomic methods to uncover genetic factors that influence individual variation in response to chemotherapy, both in terms of varying degrees of efficacy of certain cancer drugs among individuals and in the severity of side effects people suffer. The results could ultimately be used to develop more effective individualized medical interventions for cancer patients.
- A grant to Dr. Raul Bastarrachea and co-investigator Dr. Anthony Comuzzie will be used to establish and evaluate a nonhuman primate model of diet-induced obesity. Baboons have shown a natural susceptibility to the development of spontaneous obesity and type 2 diabetes. Therefore, investigators believe the animal could be a valuable new research model to advance investigations on diet-induced obesity and its related health complications. It also would benefit the development and evaluation of new drugs and experimental surgical interventions to prevent obesity.
- Dr. Robert Lanford will attempt to develop a new nonhuman primate model for hepatitis C, the leading cause for liver transplantation in the United States and the cause of one of this country's most rapidly increasing types of cancer. Currently, the chimpanzee is the only animal model for hepatitis C because it is the only animal susceptible to infection. This prohibits research on candidate vaccines and new treatments because the availability of chimpanzees is so limited. Therefore, Dr. Lanford will utilize a series of recent conceptual and technical breakthroughs to see if adaptation of hepatitis C to the baboon is possible.
- Herpes simplex virus (HSV) infects most individuals in their first few years of life and can cause a number of health complications, including diseases of the eye. Following the initial infection, it enters a dormant phase and typically remains fairly benign. However, the virus can later reactivate to cause disease again. There is no cure or vaccine for the virus, but there are antiviral treatments, the most common of which is a drug called Acyclovir. There are problems with drug-resistant HSV, especially for patients who are immunocompromised because of chemotherapy, organ transplant or AIDS. With his new grant, Dr. Anthony Griffiths will develop an improved

mouse model of Acyclovir therapy. Then he will investigate the pathogenesis of various drug-resistant viruses in the Acyclovir-treated animals. The data generated will provide information necessary to design improved HSV therapies.

- Dr. Laura Cox will use the baboon model and new genomic research methods to define specific genes that regulate the concentration of LDL, the "bad" cholesterol, in the blood. These new genomic tools provide the means to analyze genetic data in the context of biological pathways in order to define genes that are most likely to play a role in the response to dietary fat and influence cholesterol levels. The resulting data could provide new targets for pharmaceutical therapies to benefit humans who have dramatically increased risk of heart disease due to high LDL cholesterol levels.
- A grant to Dr. Susan Mooberry will enable the next step in her promising research on Texas plants as a source for new cancer-fighting drugs. With the idea that the same chemicals that make Texas plants hardy might also be useful in fighting cancer, she previously developed a library of 900 Texas plant extracts and evaluated them for their ability to kill cancer cells. Results showed that 33 of those extracts have excellent potential to yield new cancer drugs. Now she will collect and prepare several pounds of new plant material and isolate the distinct compounds that kill cancer cells so they can be used for follow-up investigations.
- A grant to Dr. Qiang Shi will be used to advance research on the use of adult stem cells derived from bone marrow to repair coronary damage after a heart attack. His work will focus in particular on a type of bone marrow stem cell, endothelial progenitor cells (EPCs), which mature into endothelial cells (cells that line the blood and lymphatic vessels and the heart). Studies in human tissues have shown that these cells can aggregate at the injury site and help form new blood vessels. However, due to the variety of EPCs and the diverse methods used to prepare them, outcomes in clinical use have been inconsistent. Therefore, it is essential to define the optimal cell source, dosage and infusion methods before this stem-cell-based therapy can be developed to treat human patients. Dr. Shi's new study will use the baboon model to help address some of these important issues.

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.

On Oct. 29, SFBR thanked Golden Circle members for their partnership in scientific progress by hosting a reception and "virtual visit" to the Foundation's campus. Members gathered under a magnificent tent outside The Argyle for a beautiful evening of dinner, drinks, and one-on-one conversation with SFBR scientists to discuss their



groundbreaking research. After a welcome and thank you from SFBR Chairman J.R. Hurd, guests had the opportunity to stop by table displays highlighting the work of the Foundation's various research departments, where they could ask questions of SFBR scientists at their leisure. *A few photographs from that memorable evening are provided here.*

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 SFBR Chief Development Officer 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.

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Spouse's Name

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Home Phone Business Phone

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Business Address ☐ Check if preferred mailing address

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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.**

A Golden Visit



Founder's Council events demonstrate the adventure of biomedical research

From flowerbeds to spacesuit labs, SFBR scientists are using every resource at their disposal to find cures for the deadly diseases that plague our world. That was apparent at recent Founder's Council lecture luncheons, which highlighted the diversity of life-saving research at SFBR and the scientific imagination that feeds it.

During the summer, members gathered at The Argyle for an update on Dr. Susan Mooberry's innovative cancer drug discovery program, and they learned that the next great cancer treatment may very well lie in their own backyard.

Many modern drugs, including various chemotherapies, are derived from natural sources, so Dr. Mooberry's search for new, less toxic ways to fight cancer has long focused on various forms of plant and marine life. Following some highly promising findings with such exotic sources as the bat flower plant and the mushroom sponge, she was inspired to examine the plants of Texas. The same chemical properties that make Texas plants hardy might also be useful in fighting cancer, she reasoned. So with the sweat of her brow and a variety of donor funding sources – including a Steves Award from the Founder's Council in 2006 – she collected and tested a vast array of Texas plant samples, first from her own yard and later from the San Antonio Botanical Gardens.

At the lecture luncheon, she informed members that she has examined more than 900 Texas plant extracts to date, testing them for their ability to kill cancer cells, and she's had the highest "hit rate" ever seen in her laboratory. She's showing that Texas plants are more than pleasing to the eye – or aggravating to the sinuses – as she conducts follow-up investigations with more than 30 of the most promising extracts. Many thanks go to Broadway Bank for sponsoring this fun and hopeful event.

The topic was no less inspiring on Oct. 10, when members gathered to hear Dr. Ricardo Carrion Jr. explain the latest developments in the Foundation's biodefense initiatives. Dr. Carrion manages the Foundation's biosafety level 4 (BSL-4) laboratory, the only privately owned maximum containment laboratory in the United States. As such, it plays a vital role in research on deadly pathogens for which there are no drug treatments or vaccines.

Viruses such as Ebola, Lassa and Marburg might not be household words, but they've caused deadly disease outbreaks in Africa, and the U.S. government is concerned that terrorists might try to use them as weapons in a biological attack. Luncheon guests were encouraged to hear about the



SFBR researcher and luncheon speaker Dr. Susan Mooberry visits with Founder's Council board member Chris Cheever.



Enjoying social time at a recent Founder's Council luncheon are (L-R) board member Jill Vassar, member Stephen Archer, president Liesl Noble, and past board member Mary Ellen Archer.

dedicated work – and particularly the promising findings – of Dr. Carrion and his peers as they continue to test novel therapies and candidate vaccines for these and other deadly agents. Goldman Sachs and Noble Inns teamed up to sponsor this compelling luncheon.

The mood was more lighthearted at a member appreciation reception at Paloma Blanca Mexican Cuisine on Nov. 8, sponsored by McNelis + Associates, and at the council's holiday party at the Tobin Estate on Dec. 5, sponsored by the Tobin Endowment and DPT Laboratories, Ltd. The council uses its annual holiday gathering to provide grant awards, typically for laboratory equipment, to advance the work of SFBR scientists. Look for information about the 2007 grant recipients in the next issue of *Progress*.

Are you interested in joining the Founder's Council, or would you like information on upcoming events? Contact Amy Abdalla at 210-258-9409 or amy@sfbr.org, or log onto the council's Web site at www.sfbr.org/pages/founder_council.php.

'Mystical Living Gardens' Gala yields large investment in human health

Southwest Foundation Forum donates record-setting proceeds to biomedical research

The Southwest Foundation Forum's "Mystical Living Gardens" Gala in May 2007 produced a bountiful harvest, generating revenues that allowed the group to make its largest gift ever – \$267,500 – to support the life-saving work of SFBR.

Now that gift is expected to spawn exciting returns of its own, as it is being used to fund 10 new pilot studies by SFBR scientists with innovative ideas for defeating such human health problems as cardiovascular disease, malaria, osteoporosis, prostate cancer, anthrax infection, and a genetic disorder called cystinosis.

"This will truly be a gift that keeps on giving," said SFBR President John C. Kerr as he accepted the Forum's donation during a morning reception at The Argyle on Sept. 13. "Pilot study funds provide the seed money needed for our scientists to initiate an innovative research program and show that a novel idea has merit. Results from these studies are then used to leverage larger grants from organizations such as the National Institutes of Health and carry those projects forward on a grander scale for the ultimate benefit of human health.

"We're most grateful to the dedicated women of the Southwest Foundation Forum, who volunteer throughout the year to support our research organization and its vital mission," Kerr continued. "The hard work and creativity they put into their spring gala will long be remembered, not only because they threw a spectacular party, but because they helped change people's lives for the better."

On hand to make the presentation to Mr. Kerr and to SFBR Chief Development Officer Corbett Christie were 2007 Gala Chair Terry Gouger, Gala Co-chair Jean Mitchell, Gala Assistant Julie Zacher, and Southwest Foundation Forum 2006-2007 President Brooke Connolly.

"It's thrilling for us to present this gift to SFBR and its scientists," said Connolly. "I'm proud of our Gala Committee, headed by Terry Gouger, Jean Mitchell and Julie Zacher. They surpassed all expectations, planning the most successful fundraiser in Forum history. I'm even more thrilled by what that means to people in San Antonio and around the world who will ultimately benefit from the research this money will sponsor."

Gouger, whose idea for establishing a "Gala Grants" program allowed donors to contribute directly to the Forum's

► *Continued on page 30*



Guests enjoy the fabulous "Mystical Living Gardens" 2007 Gala.





Forum, continued from page 29

gift to SFBR, expressed her gratitude to the many individuals and corporations who helped make the event so successful. It broke the previous Forum record by more than \$100,000. "Without the help of dozens of volunteers, and without the financial contributions of countless individuals and corporations, we never could have achieved something this significant. Thanks to all who helped us make this gift to human health," she said.

The 10 pilot studies funded by this Southwest Foundation Forum gift are for approximately \$25,000 each and target a myriad of health problems.

In the area of cardiovascular disease:

- Dr. Amanda Vinson aims to uncover how genes influence inflammation of the heart and arteries and how inflammation ultimately contributes to heart disease. Specifically, Dr. Vinson will search for genes that influence a number of pro- and anti-inflammatory proteins (cytokines) secreted by cells of the immune system that regulate inflammation in heart disease. She will investigate genetic effects on variation in these cytokines and correlations in the baboon model.
- Dr. Laura Cox will follow up on preliminary research indicating that two carboxylesterase (CES) enzymes active in the liver and intestines may influence individual variation in HDL and LDL cholesterol levels. She will do a detailed analysis of these enzymes to identify all their genetic variations, then analyze these variations within the context of data obtained on the Foundation's pedigreed baboon colony. This will help determine whether any of these variations influence HDL and LDL cholesterol levels, and if so, which particular variants are involved. That knowledge could provide new drug targets for cholesterol regulation.



- Dr. Jac Charlesworth will do a detailed examination of the five most significant genes from a set of 150 that SFBR investigations have shown to have a strong correlation with plasma total antioxidant status (TAS). Plasma TAS is a measure of the current state of oxidative stress in an individual, and oxidative stress is a major risk factor for atherosclerosis (hardening of the arteries) and cardiovascular disease. Dr. Charlesworth's findings should advance understanding of the mechanisms behind cardiovascular disease, which could lead to improved treatments.
- Dr. Sue Rutherford will follow up on findings that a gene or genes in a single region of chromosome 11 are tied to blood pressure changes in Mexican Americans. She will analyze three gene regulatory regions within this portion of chromosome 11 to identify the genetic changes responsible for increased susceptibility to high blood pressure. Results may lead to better methods of controlling high blood pressure, which is a major risk factor for coronary heart disease and stroke and is associated with renal disease, insulin resistance, diabetes, and peripheral vascular disease.



In the fight against malaria:

- Dr. Tim Anderson will isolate malaria parasites that have developed genetic mutations that make them resistant to anti-malarial drugs, then sequence and analyze their genomes to determine which genetic mutations are responsible. His

findings will allow scientists to develop simple tests for tracking the spread of drug-resistant malaria in the field and to redesign malaria drugs to restore their effectiveness. Every year, more than 500 million people in 90 countries get malaria, and 1.5 million to 2.7 million die from the infection. Death tolls are rising because the mosquito-borne parasites that cause malaria have developed resistance to all but one of the drugs widely used to treat the disease.



Forum and SFBR representatives gathered at The Argyle in September to celebrate the gala's great success. Shown participating in the Forum's official check presentation to SFBR are (L-R) Jean Mitchell, gala co-chair; Brooke Connolly, Forum president in 2006-2007; Julie Zacher, gala assistant; Terri Gouger, gala chair; John C. Kerr, SFBR president; and Corbett Christie, SFBR chief development officer.

- Dr. Susan Mooberry will screen 1,100 extracts from 366 Texas plant species for activity against malaria parasites, with the ultimate aim of finding a source for new anti-malarial drugs. Dr. Mooberry developed her extensive collection of plant samples with the idea that chemical properties that make Texas plants hardy might also make them useful in fighting diseases such as cancer. Building upon success in that effort, she is now teaming up with Dr. Tim Anderson to test the plant extracts' ability to kill malaria parasites. They have reason to hope for success. Two malaria drugs – artemisinin and quinine – are derived from plants.



In osteoporosis research:



- Dr. Lorena Havill aims to validate a novel application of a genetic research method known as transcriptional profiling in the search for genes that influence bone health. Her pilot study will utilize samples obtained from the Foundation's pedigreed baboon colony and a new genetic discovery

method developed by SFBR scientists to improve understanding of the genetic regulation of bone tissue. Ultimately, this will facilitate earlier identification of persons at greater risk for bone fracture due to osteoporosis-associated skeletal fragility and inform future development of more effective prevention and treatment strategies.

In research on the diagnosis of prostate cancer:

- Dr. James Mubiru will study the baboon as a new animal model for research on individual variation in prostate-specific antigen (PSA) levels. PSA levels are important in the diagnosis of prostate cancer, but there are problems with the test, since 25 percent of men with high PSA levels do not have cancer, and about one quarter of men with prostate cancer do not have high PSA levels. Therefore, clinicians need help in understanding non-cancer-related reasons for individual variation in PSA levels. Because baboons are similar to humans in genetics and physiology but do not develop prostate cancer, Dr. Mubiru believes that studies with these animals could help explain what other factors influence PSA levels. He will look specifically at differences in genes, age, and body fat and obesity.

In research on the single-gene disorder cystinosis:

- Dr. Katy Freed will generate cell lines from blood samples obtained from families affected by cystinosis, then use those cell lines to search for genetic discoveries that could be used to develop new or improved cystinosis treatment methods. Cystinosis is a rare metabolic disease caused by disruption of the *cystinosis* gene, which is needed to transport the amino acid cystine out of cells. Without a specific and difficult treatment regimen, cystine accumulates to toxic levels and slowly destroys the organs in the body, including the kidneys, liver, eyes, muscles and brain.



In biodefense efforts against anthrax:

- Dr. E. Ellen Schwegler's study could help provide a new method of detecting, diagnosing and treating anthrax infection. She will use proteomic technologies to determine whether anthrax infection produces distinct proteins, or protein signatures, that are detectable in blood plasma. These protein signatures could provide a mechanism for detection or prediction of anthrax infection. They may also aid in the development of better anthrax vaccines and treatment options.

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 more than 75 doctoral-level scientists work together on approximately 200 major research projects.

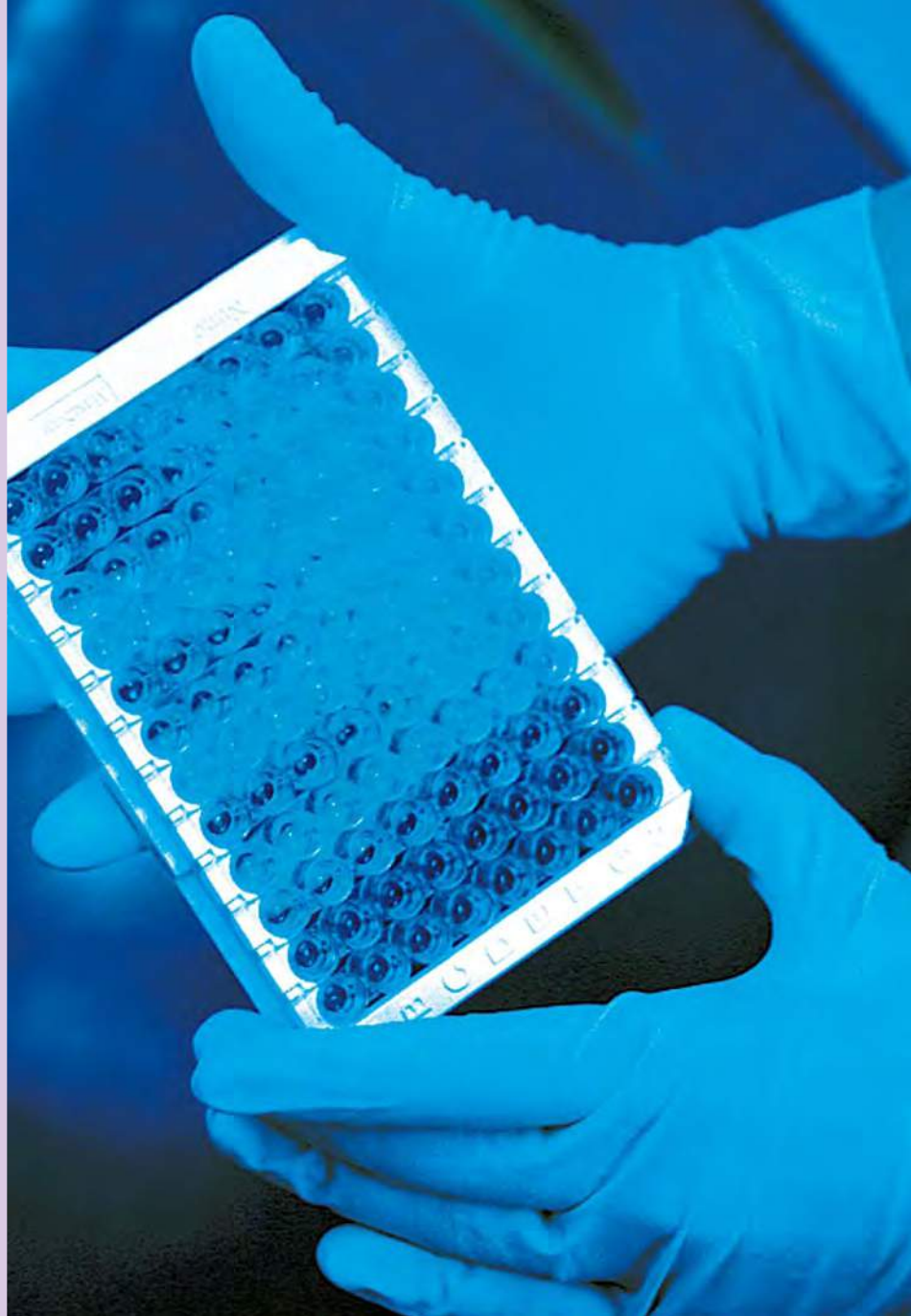
Located on a 332-acre campus in San Antonio, Texas, Southwest Foundation partners with hundreds of researchers and institutions around the world, targeting advances in the fight against heart disease, diabetes, obesity, cancer, hypertension, psychiatric disorders, AIDS, hepatitis, malaria, parasitic 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 dedicated to human 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. Approximately 65 percent of its annual budget is funded from highly competitive, peer-reviewed federal research grants and contracts, while another 11 percent comes from commercial contracts with biotechnology and pharmaceutical firms. Philanthropy constitutes the second-largest portion of the Foundation's budget, as nearly a quarter of SFBR expenses are met by the generous contributions of foundations, corporations and individuals, as well as income and royalties from SFBR's 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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