SFBR
PROGRESS
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Hope springs from discovery

Could Texas plants help fight cancer?

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Message from the President

Anthony J. Infante, M.D., Ph.D.

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Just one year into my presidency at SFBR, I realize my good fortune in leading an institution already familiar with success. A unique set of extraordinary scientific resources is in place to propel the visionary research of expert faculty who already have contributed to medical breakthroughs. The vaccine we have for hepatitis B and some of the therapies used to save the lives of premature infants are two things that come to mind.

I see my charge as helping the organization build upon its strengths and accomplish even greater things for human health in the future. It is for this purpose that SFBR is now engaged in a comprehensive strategic planning process that is a cornerstone of my presidency. Faculty, staff and board members have been working hard to develop a shared vision for SFBR that will guide us in the next five years. I would like to take this opportunity to share with you some personal perspectives on our progress to date.

First, we have clarified our focus by refining our mission statement: *"SFBR is dedicated to advancing the health of our global community through innovative biomedical research."*

Dedication to this mission is one thing that characterizes SFBR at all levels. We believe deeply in what we do. We recognize that we are part of an effort to improve the health and welfare not only of our own families and local communities but of people around the globe. SFBR is a place of innovation, where we are not content to make marginal progress but strive to make a real impact on major health problems.

In pursuit of that mission, we want to achieve the following in the next five years:

International recognition of SFBR scientists. Superior results can only be achieved by recruiting, developing and retaining superior scientists. We aim to have tangible recognition of our faculty by the U.S. National Academy of Sciences and the Howard Hughes Medical Institute, as well as through other memberships and awards.

An efficient, supportive, team-oriented culture. We will achieve more with scientists, administrators and support staff working together. Biomedical research is increasingly done in teams, and SFBR needs to be at the leading edge of this trend.

An up-to-date campus that supports our unique scientific resources. I call this the Southwest Airlines approach, finding and exploiting unique niches. In addition, despite our previous successful capital campaign, many parts of our campus are still in need of updates and upgrades.

Leveraging our strengths through strategic partnerships. While individual SFBR scientists actively collaborate with others from across the country and around the world, we can amplify our results by entering into institutional partnerships in support of shared strategic research directions. We will look for opportunities to complement the scientific capabilities of SFBR with those of other institutions in ways that enhance our research programs.

Financial stability with expanded and diversified financial resources. While this goal speaks for itself to some extent, one important outcome will be to give SFBR the flexibility to develop new ideas, make capital investments, and recruit and retain top scientists. These items are usually not fundable through NIH grant or contract funding.

Breakthrough scientific results. This is our bottom line as a research institute. The other five goals are all aimed at creating the breakthroughs that will make a difference in the health of our families and communities. We will do this by laying the foundation for new methods of diagnosis, treatment and prevention.

As you go through this issue of *Progress*, you will read about a number of exciting projects designed to break new ground in the fight against major illnesses:

- Dr. Susan Mooberry's use of Texas plants in the search for new and improved ways to treat cancer
- Dr. John VandeBerg's new program to test a promising vaccine against tuberculosis
- Dr. Tony Comuzzie's project to find genes that influence susceptibility to obesity – and his team's findings about how the obesity epidemic is taking its toll on children's health
- Dr. Lorena Havill's search for genes that influence our risk for osteoporosis, with the ultimate aim of finding new preventions and treatments

As you learn about these and other compelling investigations at SFBR, I think you will agree that Foundation scientists are well on their way to generating the breakthrough results we envision in many areas.

Can Texas plants help fight cancer?

Could a great new cancer drug be found in your own backyard, perhaps in the leaves of the Nandina, the bloom of a beautiful Texas wildflower, or even the roots of a troublesome weed?

A novel research project led by Dr. Susan Mooberry is exploring this question, and early test results indicate that it's certainly possible.

Dr. Mooberry directs a cancer drug discovery program at SFBR, where she studies numerous types of plant and marine life in the search for new compounds to provide more effective, less toxic ways to fight cancer.

Over the past few years, she has found promising results with compounds derived from such exotic sources as the tropical Bat Flower plant and a marine organism known as the chocolate sponge or mushroom sponge.

Now she has set her sights on plants that thrive in Texas, thinking that the same chemical properties that give Texas plants their hardiness might also be useful in fighting cancer. "We're looking at things that are tough, plants that are drought resistant, deer resistant, resistant to mildew and other fungi," Dr. Mooberry said. "These are some hints we're taking from nature. For example, why don't deer eat certain plants? Well, they probably taste bad. Why do they taste bad? It must be something in their chemistry. Maybe something about that chemistry could be useful in fighting cancer, and that is what we're trying to find out."

Dr. Susan Mooberry samples Texas plants in search of cancer-fighting compounds.

So far, lab results show that her hunch is a good one. "We have evaluated 300 extracts thus far, and 11 percent of them were highly active against cancer cells," said Dr. Mooberry. "This is the highest 'hit' rate that we have ever seen in plant extracts, suggesting that the plants of Texas might be an excellent source for new antitumor agents."

Donor support, local collaborations enable novel research

This novel research began two summers ago, after Dr. Mooberry's laboratory received a pilot study grant from the Southwest Foundation Forum, which works to raise funds for and public awareness of the research done at

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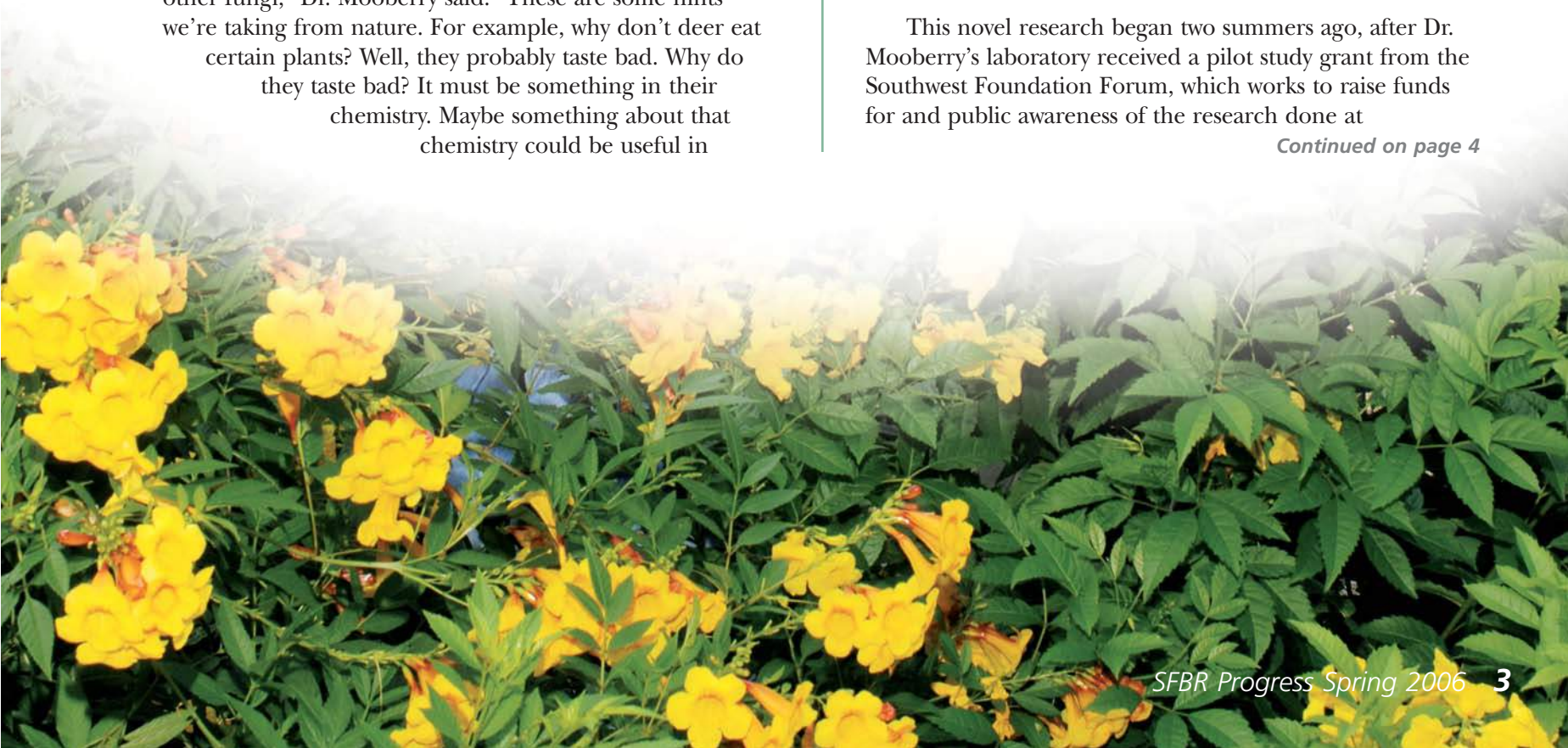

Students Mildred Abodakpi and Lauren Clark help collect plant samples from the San Antonio Botanical Garden.

Plants, continued from page 3

SFBR. Since that time, partial funding for the project's continuation have been awarded by the Amon G. Carter Foundation, the W.B. and E.G. Stuart Trust, The William Randolph Hearst Foundation and the Joe and Jesse Crump Foundation. The Helen Freeborn Kerr Foundation and the Shelby Rae Tengg Foundation also provided funding for equipment that facilitates this and other cancer drug discovery efforts in Dr. Mooberry's laboratory.

With this enabling support, Dr. Mooberry and fellow researcher Evelyn Jackson set about the task of collecting approximately 100 plant samples during the summer of 2004, mostly from their own backyards, including Texas sage, American beauty berry, Turk's cap, *Salvia gregii*, and Nandina.

Then in 2005, Dr. Mooberry began a new collaboration with the San Antonio Botanical Garden, a facility of the San Antonio Parks and Recreation Department, giving her access to an additional 200 specimens.

"With its extensive collection of Texas plants, including its new native plant trail, the Botanical Garden offers an ideal site for collecting samples," Dr. Mooberry said. "This has been a fabulous collaboration."

Dr. Mooberry explained the importance of having direct access to a large variety of plants, which allows her to collect fresh samples. "We do things a little bit differently from others in the plant community in that we use our material fresh," she said. "In the field, we actually put it in a cooler to keep it fresh and out of the sun. As soon as we bring it back to the laboratory, it's immediately frozen. We are retaining the chemical diversity by freeze-drying, whereas, sometimes if you dry things [conventionally], that diversity can be lost."

Lauren Clark, a botany student from the University of Texas at Austin, and Mildred Abodakpi, a student from St. Mary's University in San Antonio, have come on board during their summer breaks to assist with plant collection and identification of voucher specimens.

Mooberry and Jackson have then used a high-tech device called a "super-critical fluid extractor" to pull three different types of extracts from each plant sample.

"With these different kinds of extracts, we try to maximize the chemistry that we extract out of the plants," Dr. Mooberry said. "We're running various assays that can predict potential anti-cancer activity. So even though we might be looking at some plants that other groups have previously studied, our methods combining the use of fresh material and our specific biological assays provide the opportunity for some new findings."

Research yields hope

In the laboratory at SFBR, they are looking for compounds in the plant extracts that show cytotoxicity — toxicity to cancer cells — or which turn on a "cellular suicide program" by disturbing microtubules. Microtubules are cellular structures that guide genetic material into the two daughter cells during cell division. A substance that disrupts normal microtubule function inhibits cell division and signals the cancer cells to initiate their own death.

Additionally, Dr. Mooberry is working with scientists at the University of Texas Health Science Center at San Antonio to develop other mechanistic assays for evaluation of these samples. It is her team's hope that any new findings from this project will be added to the preclinical development collaborations she has ongoing with the Cancer Therapy and Research Center.

"Our early results are very promising, and we look forward to identifying the active chemical constituents in the plants of Texas that might have potential for use against cancer," Dr. Mooberry said.

She's highly optimistic that the plants of Texas are more than pleasing to the eye.

An international effort to fight tuberculosis

Novel candidate vaccine has potential to save millions of lives

With a new $3.4 million grant from the National Institutes of Health, SFBR scientists are testing a novel vaccine for tuberculosis (TB), one of the leading killers of young adults worldwide, causing 3 million deaths annually.

Dr. John VandeBerg, director of SFBR's Southwest National Primate Research Center, serves as principal investigator on the 4½-year grant, which supports the efforts of an international team of investigators.

"Dr. Celio Lopes Silva of the University of Sao Paulo [in Brazil] has taken a novel approach to designing this vaccine, which is intended to be both preventive and therapeutic, and it has already shown impressive preliminary results in mice," Dr. VandeBerg said. "It's exciting for us to carry forward his work on a vaccine that could eventually save millions of lives."

The global impact of tuberculosis

The World Health Organization considers TB among its top three priorities for infectious diseases urgently in need of research. The others are malaria, which kills more than 1 million people annually, and AIDS, which causes 3 million deaths each year.

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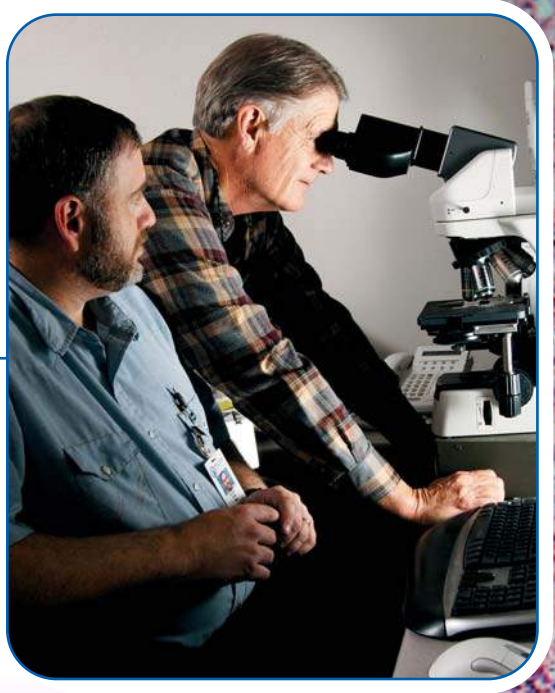


SFBR veterinary pathologists Drs. Edward Dick and Gene Hubbard examine a slide of a lymph node from a monkey naturally infected with tuberculosis.

Dr. Luis Giavedoni and other immunologists from SFBR and Brazil will study monkeys' immune response to TB and to a new candidate vaccine.

Tuberculosis, continued from page 5

The bacterium that causes tuberculosis infects 2 billion people, or nearly a third of the world's population. While the vast majority maintain latent infections that are not contagious and do not cause health problems, each year approximately 8 million develop the active, infectious disease, and 2 to 3 million die from tuberculosis. Experts believe 10 million Americans are infected, of which about 10 percent will get sick with the disease.

TB is an infectious disease that primarily attacks the lungs, although it can attack any part of the body. Symptoms of the active disease typically include a bad cough that lasts three weeks or longer, pain in the chest, coughing up blood, fatigue, weight loss, loss of appetite, chills, fever, and night sweats.

TB infections in the United States began declining in the 1940s, when effective antibiotics were introduced. However, infections have been on the rise since the mid-1980s for a number of reasons, including the AIDS epidemic – HIV and TB are common co-infections – and patients' failure to comply with the lengthy course of treatment, which can last up to a year. These factors have contributed to TB's increasing resistance to antibiotics, adding to the seriousness of the disease and increasing the need for an effective vaccine.

One TB vaccine, the BCG vaccine, is already used in some countries, but it has several shortcomings, including poor efficacy in adults, wide variation in its efficacy in children, and interference with the TB skin test. The Silva vaccine may have the ability to overcome these problems because of its novel design, including its own built-in booster mechanism.

A novel vaccine: How it could help

Dr. VandeBerg said the grant, awarded by the NIH's National Institute of Allergy and Infectious Diseases, has two major purposes: to test the Silva vaccine for its ability to prevent infection, and to test it as a therapy against an already active infection. Scientists also expect to advance the medical community's understanding of the body's natural immune response to TB infection – as well as how this vaccine affects that immune response – and to determine the appropriate vaccine dosage.

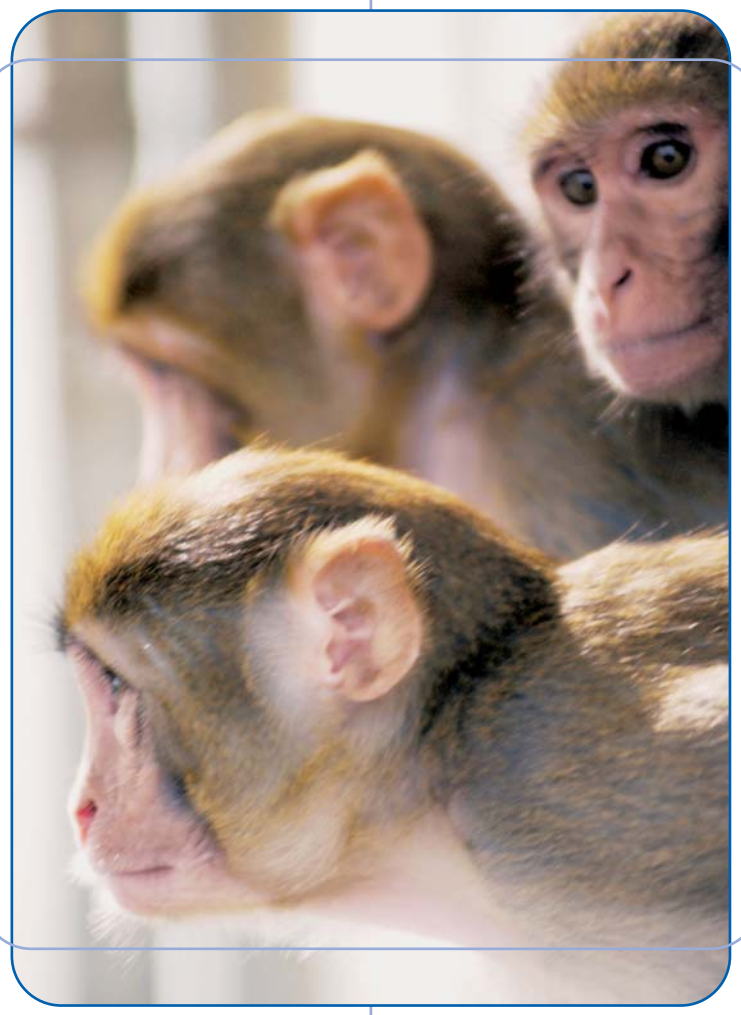
"The possibility of a vaccine that is both preventive and therapeutic could be a major advance for global health," said Dr. VandeBerg. "This vaccine could potentially be used to help control the disease in the millions of people already suffering from active tuberculosis, and it could be used to prevent billions more from becoming infected with the bacterium in the future."

Dr. Silva's vaccine is based on heat shock protein 65 (hsp65), which is isolated from the TB bacterium and stimulates an immune response when injected into animals or people. While scientists have attempted for decades to develop TB vaccines based on hsp65, Dr. Silva added some new twists.

For one, he uses microspheres of biodegradable materials that encapsulate the hsp65 protein and delay its release into the body. However, the microspheres also contain the hsp65 DNA, which is much smaller in size and can immediately escape from the microspheres. The DNA quickly starts to produce the protein, stimulating the body's primary immune response. Then, a few weeks later, after the various layers of the microsphere melt away, the hsp65

protein itself is released into the body, essentially providing a booster shot that stimulates a secondary immune response.

For added punch, Dr. Silva also incorporated a glycolipid into the vaccine formula, which enhances the body's own immune response to TB infection.



The need for SFBR resources to test the vaccine

Dr. Silva and his team have successfully tested the vaccine in various animal models, but not in nonhuman primates, whose immune characteristics are more similar to humans'. SFBR's primate center is known worldwide for the quality of its primate-based research.

This study will utilize the primate center's rhesus monkey population. Rhesus monkeys are the nonhuman primates most susceptible to developing tuberculosis. They are also the most commonly used animal model in research on HIV. This combination of characteristics will enable scientists to study the vaccine's effect on TB infection alone and in cases involving TB and HIV co-infection.

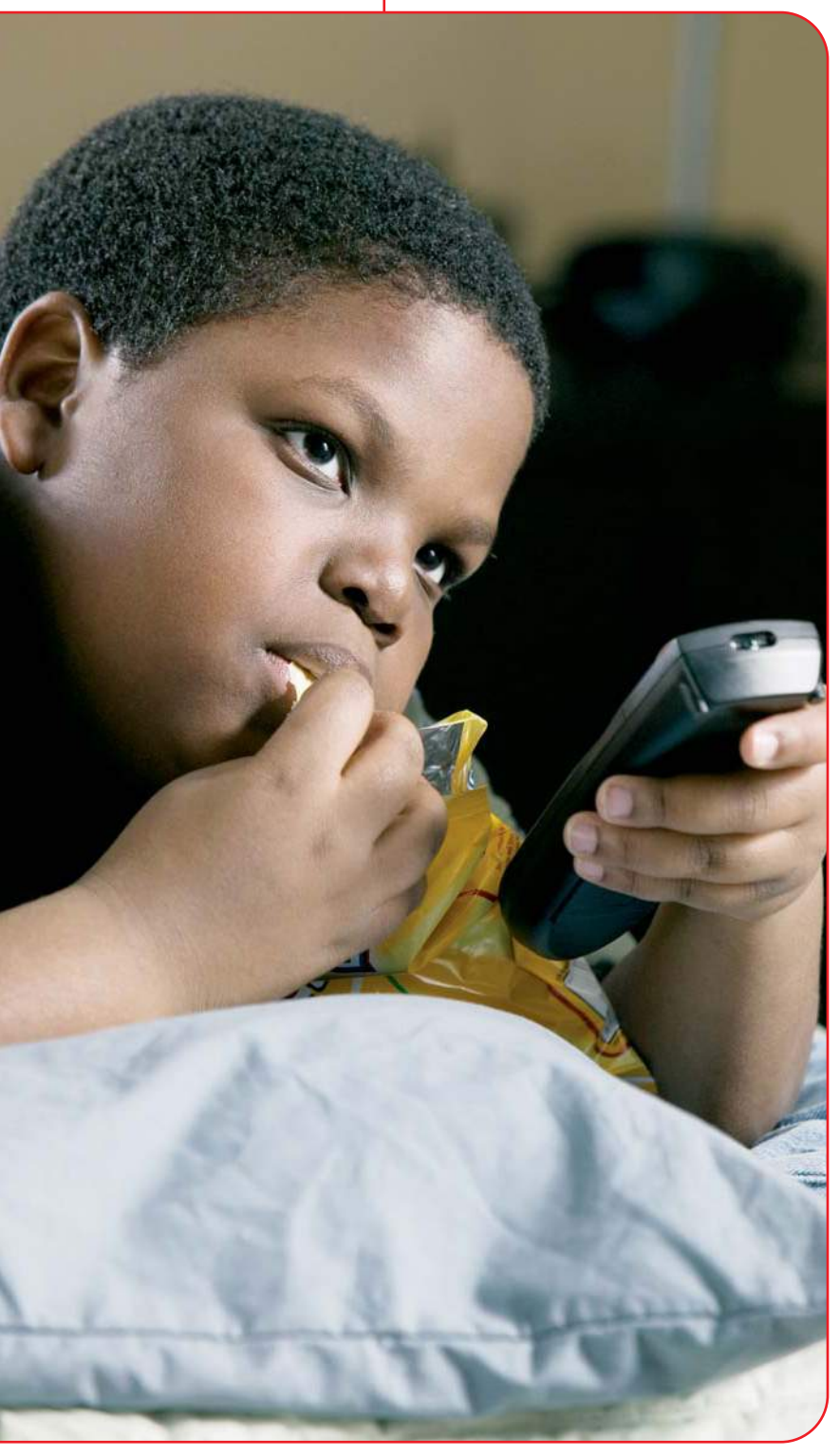
The Foundation's laboratory facilities, including two new biosafety level three (BSL-3) facilities capable of handling nonhuman primates, are also ideally suited to the project. Dr. VandeBerg believes this study will establish the expertise, technologies and other capabilities of the Southwest National Primate Research Center to collaborate with investigators from all over the world who need to test novel TB vaccines and drug treatments.

In addition to Drs. VandeBerg and Silva, other collaborators on this research project include Dr. Maria da Glória Bonecini de Almeida of the Oswaldo Cruz Foundation, Brazilian Ministry of Health, and Drs. Luis Giavedoni, Ana Cristina Leandro, Gene Hubbard and Edward Dick, all with SFBR.

Drs. Bonecini de Almeida, Giavedoni and Leandro are immunologists who will study the animals' natural immune response to the TB bacterium and to the vaccine. They also will determine the extent of immunological protection provided by the vaccine. Drs. Hubbard and Dick will provide pathology support to determine the effectiveness of the vaccine to prevent infection and to eradicate TB bacteria from the lungs and other tissues. Veterinary support will be directed by Dr. Melissa de la Garza, also with SFBR.

> **The possibility of a vaccine that is both preventive and therapeutic could be a major advance for global health.**
>
> **– Dr. John VandeBerg, Director of SFBR's Southwest National Primate Research Center**

Obesity epidemic taking toll on children's health



As summer rolls around and more people don shorts and swimsuits, many adults feel the need to shed some extra pounds. But studies show that our children need to do the same, and not just so they can fit into smaller clothes.

Findings by the first family-based study on the genetics of childhood obesity and metabolic disease shed light on how the extra pounds around children's waistlines are already triggering biological processes that make them susceptible to the early onset of diabetes and heart disease.

In the December 2005 issue of *Pediatric Research*, scientists from Southwest Foundation for Biomedical Research and Baylor College of Medicine in Houston laid out findings from their VIVA LA FAMILIA study involving 1,030 children and 600 parents from 319 Hispanic families in the Houston area. The study, which focuses on families with a high percentage of children that tend to be overweight or obese, found that 20 to 28 percent of these children – some as young as 4 years old – show the same markings of metabolic syndrome typically seen in middle-age, obese adults.

What is metabolic syndrome?

Metabolic syndrome in adults is defined as the constellation of three or more metabolic risk components that make one susceptible to diabetes and cardiovascular disease, including abdominal obesity, glucose intolerance, high blood pressure, dyslipidemia (abnormally high lipid levels in the blood), low HDL cholesterol, and hypertriglyceridemia (high triglycerides).

In this family study, metabolic syndrome was found in 20 percent of the overweight, Hispanic children ages 4-19 when five of the conventional components were included; it was found in 28 percent when abnormal liver function also was included as a risk factor.

"These findings wouldn't be surprising for a group of middle-age adults, but to see this in children is quite startling," said Dr. Anthony Comuzzie, a lead scientist on the project at SFBR. "Our study indicates that perhaps one out of every five obese children is showing metabolic risk factors associated with adult-onset disease, adding to mounting concerns that as the childhood obesity epidemic increases, we could start seeing 18-year-olds having heart attacks."

These findings wouldn't be surprising for a group of middle-age adults, but to see this in children is quite startling.

– Dr. Anthony Comuzzie, a lead investigator on the VIVA LA FAMILIA study

A collaborative study

Dr. Comuzzie designed the study in collaboration with its principal investigator, Dr. Nancy Butte of the USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine. With Baylor's extraordinary set-up for metabolic research and Dr. Butte's expertise in nutrition and childhood development, she and her research team have worked directly with the families and managed the study's data collection, phenotyping, and physiological analyses.

Meanwhile, SFBR geneticists are using their expertise and resources to find genes that might be influencing the young people's susceptibility to obesity and related metabolic disorders. Dr. Comuzzie directs the study's statistical genetics component, while another lead researcher, Dr. Shelley Cole of SFBR, oversees the genotyping and molecular analyses.

Dr. Comuzzie explained that while metabolic syndrome is not a disease in itself, the cumulative effect of the chronic presence of these risk factors eventually takes its toll on the body.

"If you have a 5-year-old who already shows signs of insulin resistance, the child's pancreas continually has to work harder and harder to produce more insulin, and by the time he reaches his teens or young adulthood, he will be more likely to develop diabetes," Dr. Comuzzie said. "Basically, the longer you live with these risk factors, the more damage is done to your system and the higher your probability of developing disease. The severity of the disease also increases."

Key risk factors and their impact

Dr. Comuzzie explained that the study shows the key risk factor to be waist circumference, saying, "What we found to be most highly associated with all the markers for metabolic syndrome was the fat that children carry around their abdomen. This seems to tie in with what other studies have shown in adults. We [the scientific community] used to think of fat purely as an energy storage depot, but we now realize that fat is probably the largest endocrine organ, producing a wide range of proteins that directly impact things such as insulin sensitivity and lipid metabolism. And abdominal fat seems to cause the most damage."

Likewise, the study showed that insulin resistance, which leads to diabetes, is a central contributor to the metabolic syndrome in overweight Hispanic children, as other studies have shown it to be in adults. It also found that the prevalence of the metabolic syndrome increased with the severity of obesity and that "the metabolic syndrome appears to emerge when a child's predisposition for insulin resistance worsens with increased adiposity (fat)."

"These are similar patterns to what is seen in adults,"

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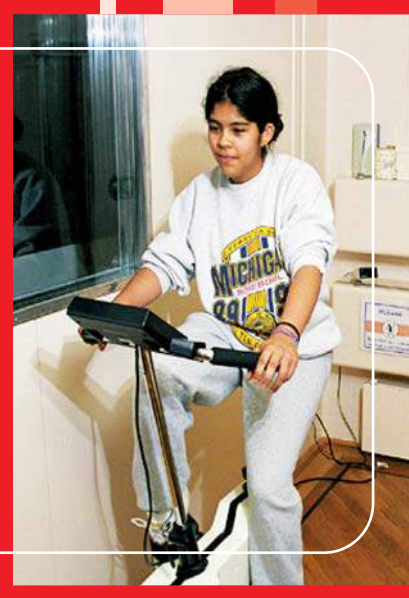
Photos provided courtesy of Baylor College of Medicine

Children's caloric expenditures and other metabolic readings are taken as they go about daily activities during a weekend stay at Baylor College of Medicine.



Dr. Shelley Cole (right) oversees molecular analyses for VIVA LA FAMILIA in her laboratory at SFBR. Here she meets with Grace-Ellen Meixner about the project.

Obesity, continued from page 9

said Dr. Comuzzie. “It’s just that in children, the wear and tear on the body gets a head start and can lead to serious health problems at an earlier age.”

The search for influential genes

He speculates that researchers also will find similar genes influencing obesity and related conditions in both children and adults, “but those who develop these problems at younger ages likely are carrying a heavier genetic burden.”

He and his colleagues are anticipating the next phase of the study, when they will further investigate some promising genetic leads. “The connection between waist circumference, insulin resistance, lipids and blood pressure, and even liver function, show they are being influenced by a common set of genes,” Dr. Comuzzie said. “We have strong evidence for common genes influencing all these risk factors, indicating that they are not genetically independent of one another. So the genes that we’re going to investigate more closely are those that show signals for overlap in these areas.”

What you can do now

Dr. Comuzzie believes that an understanding of the genetic causes of obesity and metabolic disorders could lead to new methods of prevention and treatment. But he and Dr. Butte point out that, because the environment also plays an important role, parents can take steps now to reduce their children’s risk of developing metabolic syndrome. Most important, they can make sure their children get plenty of exercise and eat a healthful diet.

“I think the hardest thing as a parent is to set a good example,” Dr. Comuzzie said. “It’s very difficult to tell your child to go outside and play if you’re sitting on the sofa. Children mimic their parents, so what you eat and how you act influences them.”

The VIVA LA FAMILIA study began in 2001 with funding from the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health. The Children’s Nutrition Research Center at Baylor College of Medicine also receives funding from the U.S. Department of Agriculture.

Looking for genetic weapons against fragile bone disease

Osteoporosis, also known as fragile bone disease because it weakens the bones and increases susceptibility to fractures, is something for which we are all at risk. Loss of bone mass is a normal part of the aging process for both men and women, with women being disproportionately affected because of the accelerated bone loss that occurs right after menopause, as the body adjusts to lower levels of estrogen.

More than 10 million people in the United Stares are currently affected by the disorder, and that number is expected to increase exponentially as the population ages.

While we are all at risk, we all can take active steps to prevent this disorder – or at least to lessen its severity – says Dr. Lorena Havill, a skeletal biologist and statistical geneticist at SFBR. While we are young, we can consume a diet rich in calcium and do weight-bearing exercise to build bone mass. After we reach our 30s, this same behavior can help us retain bone mass. Some pharmaceuticals also can help in this effort.

But can we do anything else to fend off this debilitating disorder, where in severe cases a sneeze can break a rib, or crumbling vertebrae can hunch the back and compress internal organs, affecting one's ability to eat and breathe properly? That is what Dr. Havill wants to find out, and she thinks part of the answer lies in our genes.

Why look to our genes?

Studies have shown that the same exercise can result in more bone gain or retention in one person or animal than another. The particular formation of someone's bones also affects bone strength, meaning that some individuals with less actual bone mass might still be less susceptible to fractures than others with more bone mass.

Trying to solve the mystery as to why, Dr. Havill is using some recent new grants and the unique pedigreed baboon colony at SFBR's Southwest National Primate Research Center to build a broad-based research program on the role genes play in the physiological processes that lead to osteoporosis.

Identification of these genes could offer physicians better screening tools to help determine which patients are most susceptible to osteoporosis, allowing them to focus on

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Dr. Lorena Havill prepares razor-thin bone samples for her studies on osteoporosis.

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lifestyle measures to build or maintain peak bone mass. It also could lead to improved pharmaceuticals for preventing and treating this disorder.

The search begins with baboons

The baboons at SFBR are an invaluable resource in Dr. Havill's gene hunt. Highly similar to humans in genetics and physiology, baboons naturally lose bone as they age. They also sit upright, exerting some of the same mechanical forces upon their spines as humans, and they live long lives, requiring their skeletons to undergo the same types of maintenance functions and physiological changes as human skeletons during the aging process. Female baboons also go through menopause.

Especially critical for Dr. Havill's study is the pedigreed baboon colony, on which familial relationships and health histories have been documented for six generations. These animals also have been genotyped, meaning that scientists have identified markers along their chromosomes where there is genetic variation. Researchers can look at how changes in these genetic markers correlate with different physical traits to discover which genes might be influencing susceptibility to various disorders.

Finally, with the assistance of faculty and staff in the Southwest National Primate Research Center, Dr. Havill is able to collect bone samples from these animals when they die, allowing for direct measures of bone strength.

Vital clues

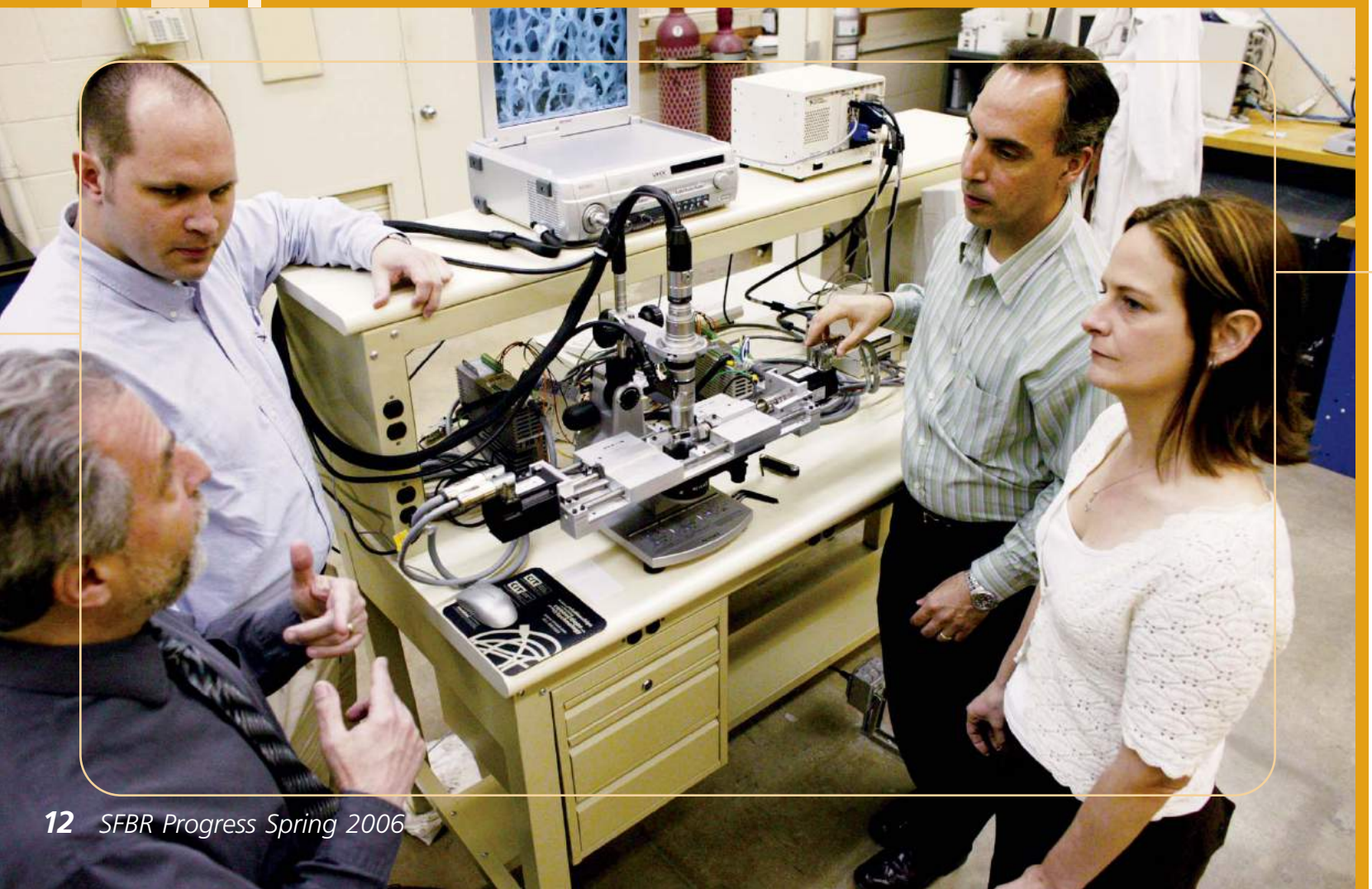
Her current efforts build upon postdoctoral work she did with Drs. Michael Mahaney and Jeff Rogers. With previous training in anthropology and skeletal biology, Dr. Havill was awarded a National Research Service Award Grant to work with Dr. Mahaney to gain knowledge and experience in statistical genetics techniques.

Together with Drs. Mahaney and Rogers, she analyzed measurements of bone mineral density collected through bone scans of nearly 700 baboons between the ages of 5 and 30 years – roughly equivalent to 15 to 90 years in humans. Bone mineral density, which is a measure of bone mass per square centimeter, is currently the best single predictor of how susceptible one is to a bone fracture.

The group's research has been highly successful, leading to several publications identifying chromosomal regions that affect levels of bone formation in the baboon and helping to establish the baboon as an animal model for research on osteoporosis.

For example, the team discovered that an area on chromosome 16 contains genes influencing levels of a

SFBR scientists Drs. Michael Mahaney and Lorena Havill (front) confer with Drs. Todd Bredbenner and Dan Nicolella at Southwest Research Institute about mechanical tests on bone strength.



substance that is secreted by bone-building cells. This genetic signal in baboons corresponds with similar findings in people involved in SFBR's San Antonio Family Heart Study. "In two primate species, we have found a genetic signal in the same place," Dr. Havill said. "That gives us confidence that we're on the right track."

New ways to learn from bones

More recently, grants from the San Antonio Area Foundation, Southwest National Primate Research Center, Southwest Foundation Forum, and Founder's Council have funded vital equipment and interns to help study other factors that affect bone strength.

For example, she is studying microscopic structures in the cortex of the bone called osteons, which form as part of normal, lifelong skeletal-repair processes.

"Human studies have shown that people who have had hip fractures tend to have more osteons, larger osteons and larger canals in the center of those osteons [than people who have not]," Dr. Havill said. "So I'm looking to see how osteon size and distribution affect bone strength as well as what role genes play in osteon formation."

Dr. Havill also uses vertebrae samples to study bone strength and susceptibility to fractures. For this, she collaborates with Drs. David Burr, Charles Turner and Matt Allen at the Indiana University Medical Center and with Drs. Dan Nicolella and Todd Bredbenner, engineers at the Southwest Research Institute in San Antonio, renowned experts in mechanical testing.

Does pregnancy play a role?

Does a woman's reproductive history influence susceptibility to osteoporosis? Human studies in this area have been contradictory, and Dr. Havill believes that may be because some women are genetically predisposed to liberating bone from their skeleton during pregnancy and breastfeeding. "That may be good for the calcification of the fetal skeleton, but it could cause problems for you later in life, when you don't want to be efficient at bone loss," she said.

To test her theory, Dr. Havill has been looking at this issue in baboons at SFBR, and she is producing some of the first evidence showing an interplay between genetics and reproductive history in susceptibility to osteoporosis.

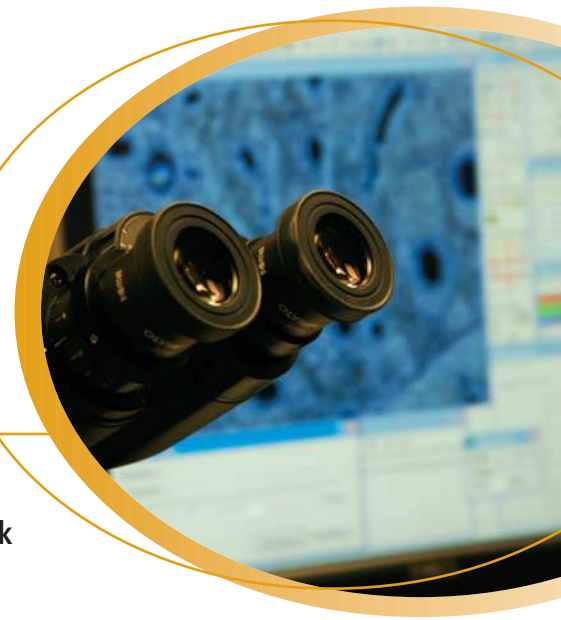
The reason for the mission

All these aspects of her research are part of an effort to better understand how the amount and arrangement of bone tissue affect susceptibility to fractures, and in turn, how genes influence this entire process, all for the ultimate benefit of developing new ways to screen for, treat, and prevent osteoporosis.

"I've seen in my own family how osteoporosis can impact virtually every single minute of your day. You adjust your entire life out of fear of coughing and breaking a rib or falling and breaking your hip," said Dr. Havill. "With the population aging worldwide, the number of people coping with this condition is going to increase exponentially in the near future. I want to learn more about this disorder, which is not well understood, so that we can do more to prevent and treat it."

A baboon with osteoporosis.

Testing bone samples from deceased animals.



A closer look at osteons.

Stay hydrated to minimize PAIN

Pain & Thirst

Recently, 10 volunteers were given saline injections to increase their thirst as researchers applied mild, intermittent pressure to their thumbnails. The researchers discovered that, as people became thirstier, they felt more pain, even though the same level of pressure was placed on the thumb.

If you're already dealing with any type of physical pain, whether it be chronic pain from arthritis or temporary pain while recovering from an injury, you'll probably want to drink plenty of water to avoid making matters worse.

In a study on the relationship between thirst and the brain, researchers have discovered that a person who is thirsty experiences pain more intensely than someone who is well hydrated. The reason is that different areas of the brain are activated when we are both thirsty and in pain as opposed to when we are thirsty only or in pain only, and these different brain signals influence our perception of which physical need or sensation most deserves our attention.

As Dr. Robert Shade, the SFBR scientist involved in the study, told the *San Antonio Express-News*, "The brain has to provide a means for allowing you to make a decision as to what is the more important thing for you to pay attention to. Where in the brain does this happen? We found an area of the brain where all of this is integrated, and some weight is put on to which is the most important signal to pay attention to."

Dr. Robert Shade (left) collaborates on an international study on the relationship between thirst and the brain.

Dr. Shade was describing results from a study on which he collaborates with Dr. Peter Fox at the Research Imaging Center at the University of Texas Health Science Center at San Antonio and with several scientists in Australia: Dr. Michael J. Farrell of the Howard Florey Institute and the Center for Neuroscience at the University of Melbourne; Dr. Derrick Denton, Howard Florey Institute and the Baker Heart Research Institute at Alfred Hospital in Prahran, Victoria, Australia; Dr. Gary F. Egan, Howard Florey Institute and Center for Neuroscience; and Dr. John Blair-West, Department of Physiology, University of Melbourne.

Working with a group of both young and elderly volunteers in San Antonio, the group is searching for answers about why our sense of thirst declines as we age. As part of this overall investigation, they use Positron Emission Tomography (PET) scans to study the relationship between the brain and various aspects of thirst.

Recently, 10 of the younger volunteers were given saline injections to increase their thirst as researchers applied mild, intermittent pressure to their thumbnails. The researchers discovered that, as people became thirstier, they felt more pain, even though the same level of pressure was placed on the thumb.

Likewise, concurrent PET scans showed changes in brain response. An area of the brain that showed no response when someone experienced only one of the sensations "lit up" when the person experienced both thirst and pain. Investigators believe this could be "where the brain integrates competing sensations and makes judgments on which is more important," they told the *San Antonio Express-News*.

Their research results were published in a February issue of the *Proceedings of the National Academy of Sciences*. The ongoing project is supported by the Robert J. Jr. and Helen C. Kleberg Foundation, the G. Harold and Leila Y. Mathers Charitable Foundation, the Brown Foundation, the Search Foundation, and the National Health and Medical Research Council of Australia.

New developments with promising treatment for anthrax

Antitoxin could provide single cure

Dr. Ricardo Carrion Jr. conducts anthrax investigations at SFBR.

A serendipitous discovery with a possible new treatment for anthrax has shown that it has even greater potential than was originally expected. Scientists now believe it could be used as a single therapy to cure both early- and late-stage anthrax infection.

Currently, antibiotics are available to kill anthrax bacteria – an effective therapy when someone is at the early stage of infection – but nothing is available to fend off the deadly toxins those bacteria produce once in a person's system. Those toxins are to blame for the death of individuals who reach late-stage infection.

Previous research by Dr. Jean Patterson's laboratory at SFBR showed promising results with a high-affinity antibody, or anthrax antitoxin, designed by the laboratories of Drs. Brent Iverson and George Georgiou at the University of Texas at Austin. In experiments with lab rats that had been infected with anthrax toxin, the antibody was highly effective at binding with the toxin and removing it from the body. It saved 100 percent of lab rats treated with the antitoxin, leading researchers to believe that it could potentially be coupled with antibiotics to successfully treat humans.

After those initial tests, UT scientists modified the antitoxin to make it last longer in the body. SFBR scientists then tested this modified version in guinea pigs that had been challenged with anthrax spores, mimicking a natural exposure to this bioterror threat. In those experiments, they found that, not only did the antibody eliminate the deadly anthrax toxin, but it also eliminated the bacteria.

In two separate experiments in SFBR's biosafety level 4 laboratory, the guinea pigs were given anthrax doses 250 to 625 times a typically lethal dose. After 72 hours, those not treated with the antitoxin succumbed to infection, but those

Continued on page 16

What we have found is that you may not even need the antibiotics to beat anthrax.

— Dr. Brent Iverson, the University of Texas at Austin

Anthrax, continued from page 15

that received the treatment remained healthy two and three weeks later, with no evidence of disease.

"What we have found is that you may not even need the antibiotics to beat anthrax," said Dr. Iverson. He said that the new treatment "looks promising" and that it could lead to a simpler and cheaper way to treat anthrax. The new antibody is produced in bacterial cells, rather than the more expensive mammalian cell culture currently used to produce anthrax antibodies.

Dr. Patterson added, "A concern to national defense is that terrorists might design a strain of anthrax that is resistant to antibiotics, but this antitoxin could eliminate those concerns by providing an effective treatment that doesn't require antibiotics."

Currently, the researchers are conducting additional tests to determine how the antitoxin eliminates anthrax bacteria, which is still unknown. They have two hypotheses, which might both be part of the full story. One hypothesis is that the antitoxin somehow neutralizes anthrax bacteria and prevents it from replicating. The other looks to innate immunity, theorizing that since the high-affinity antibody clears the body of the deadly toxin, it allows the body's initial immune response to successfully kill the anthrax bacteria on its own.

This research is sponsored by the National Institute for Allergy and Infectious Diseases and the U.S. Department of Defense.

From her office, Dr. Jean Patterson monitors anthrax experiments underway in SFBR laboratories.

In the spotlight:

Trustee Ronald Calgaard, Ph.D.

In each issue of Progress, *we highlight one of the members of SFBR's stellar Board of Trustees. For this issue, the editor visited with Dr. Ronald Calgaard, who retired in 1999 as the longest-serving president in the history of Trinity University. Credited with bringing a vision to the school that led it to national prominence, Dr. Calgaard also has made his mark on numerous local businesses and civic organizations through his various community involvements. Here, he offers particular insights into how his time at Trinity parallels with SFBR's current efforts to reach for even higher levels of achievement.*

In 1979, when you came from the University of Kansas to take the helm as president of Trinity University, the school was in a time of transition and seeking to clarify its mission. Would you tell us about the vision you brought to the school?

I thought Trinity was in a wonderful position to become a truly first-rate undergraduate liberal arts college that was residential in nature. The Midwest and the Northeast had many institutes of this type, but it was the kind of institution that hadn't really developed in the Southwest. So the goal was to make Trinity a distinctive institution, the No. 1 undergraduate liberal arts institution in this part of the country and among the best in the nation.

We set out very strongly to accomplish that objective, and there were some unique things we did in the process. We got smaller rather than bigger. We got out of some graduate programs that we didn't think were strong. Admission standards increased rather significantly over time. We started building the human resources that would support the kind of institution we were trying to be, endowing distinguished professorships and recruiting great faculty to fill them, and we worked to build up the library. We became an aggressive recruiter of high-quality students, eliminating athletic scholarships but putting large amounts of money into merit scholarships. Consequently, we went from 10 or 12 National Merit finalists in our freshman class to over 100 in the freshman class within two years.

We went through a real culture change through the mid-1980s, and naturally this caused a little bit of tension. Not everyone was enthused, but for the most part, things went very well. After that, we had a clear vision of what we were trying to be, and people on campus were very focused on achieving those objectives. Before long, we garnered the national recognition we sought.

There are parallels between your story and SFBR today. The institution has a new president who is guiding it through a strategic planning process, trying to focus its vision for the coming years and guide it to an even higher level of achievement. As an executive committee member on the Foundation's board, you are playing an active role in this process along with faculty and staff.

Yes, and I believe the timing is right for this. There is a new president, Dr. Tony Infante, who comes with both a clinical medical background and a research background, giving him the type of insight necessary to be a good leader

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Calgaard, continued from page 17

for a unique institution like the Foundation. The Foundation has made real progress both in terms of its basic infrastructure and the development of its resources, such as the Southwest National Primate Research Center, its tremendous genetic resources, and other assets. It has outstanding senior faculty, and probably over the next few years, there will be the opportunity to recruit a few more. The financial base of the institution has broadened. So the prospects are good for the Foundation to excel.

Still, there are challenges. The development of a good strategic plan – defining what we want to look like five to 10 years from now and establishing clear objectives for meeting our goals – should make us more effective in overcoming those challenges.

Just as at Trinity we saw that we couldn't be all things to all people, the plan at the Foundation is to focus on those things that we can do very, very well and strive to be leaders in those fields where we think we can be dominant.

To do this, we're going to have to meet some of the same requirements we did at Trinity. For example, we're going to have to raise a significant amount of endowment money. We can't be quite as dependent upon the National Institutes of Health and other sources of federal funding, although those will always be terribly important to an institution like the Foundation. All medical research around the country is attracting enormous resources, so we're going to have to raise significant private dollars to support our agenda of biomedical research. Some of that will have to be cooperative between the Foundation and other local institutions such as the UT Health Science Center, UTSA and others interested in biomedical research.

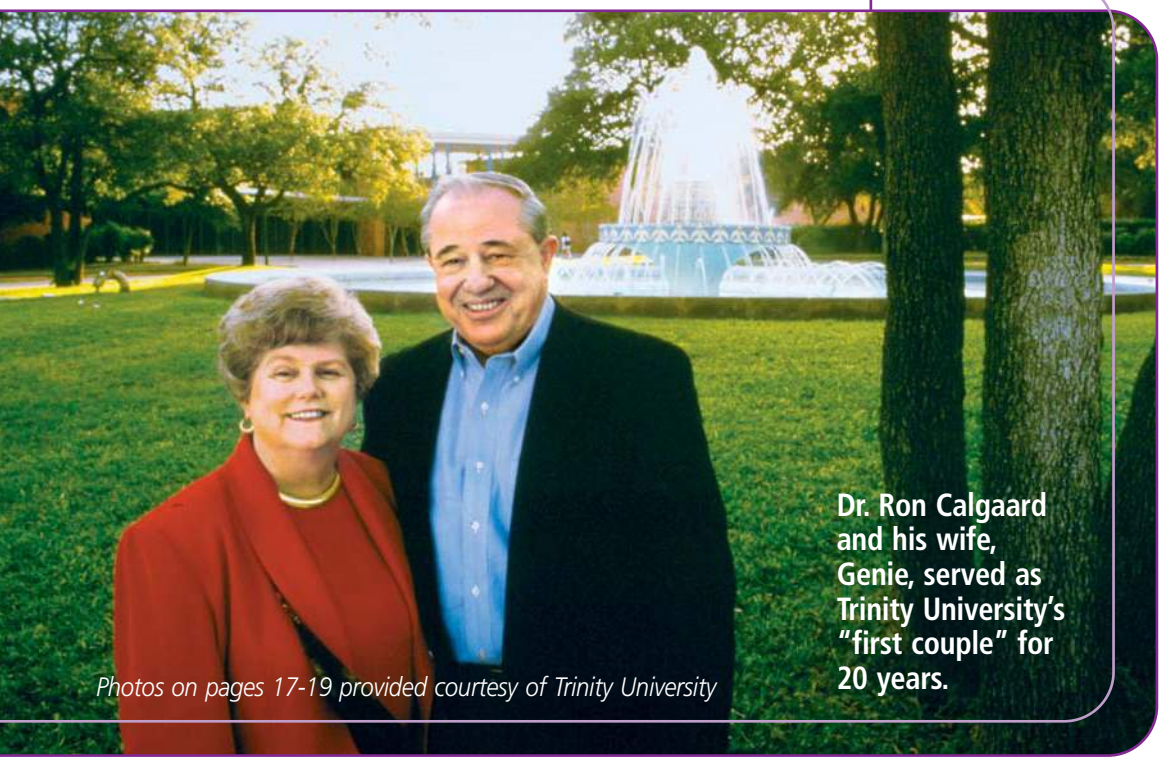
Fundraising was a big focus of yours at Trinity. Under your leadership, the university quadrupled its endowment and added more than $100 million in new or renovated facilities to its campus without incurring long-term debt. People describe you as having tremendous insight into fundraising.

Fundraising is not all that complicated. You need to have a clear and precise mission with which people can identify; your vision has to be sufficiently challenging and exciting so that, if you accomplish it, you will truly have done something of significance; and you've got to be able to tell your story so that people understand that their gifts will make a difference in helping the institution to achieve important objectives. In addition, every president has to have the benefit of a strong board that is really committed, which was a great blessing I had at Trinity.

It's been said that one of the keys to your success was your wife, Genie, who is acclaimed as one of Trinity's great "first ladies."

Oh, yes. As a college president, especially at a residential institution, you need a spouse who clearly likes people and enjoys the process – not every day, but almost all the time – and who loves to entertain. In the course of any year, we would host 5,000 or 6,000 people in our home for receptions and dinners. It was a fascinating experience, hosting everyone from Trinity students to U.S. presidents and other heads of state such as [then British Prime Minister] Margaret Thatcher. Some were much better house guests than others, but Genie took wonderful care of them all.

To this day, I suspect that my spouse sends birthday cards to all the former Trinity trustees. That is just how she is. And the building and grounds crew at Trinity would do almost anything in the world that my wife asked of them. They loved her. Why? She knew all their names. She would have them over to the house. That is a real gift of hers. She makes every person feel very important.



Dr. Ron Calgaard and his wife, Genie, served as Trinity University's "first couple" for 20 years.

Photos on pages 17-19 provided courtesy of Trinity University

You kept such a busy schedule as Trinity's president, and yet you stayed on for 20 years, the longest tenure of any president in the school's history and far above the current national average. Most college presidents today serve five to seven years. What gave you the drive and commitment to stay on for that length of time?

I have no problem with the drive. I suspect I have an unusual metabolism. I'm a high-energy, classic "A type," a bit of a risk-taker who has always been interested in challenges just to see if I could accomplish them. I also had the good fortune to become president at a relatively

Dr. Calgaard visits with Flo Crichton, former President George Bush and Trinity University students before the former president's speech at the Cameron Lecture on Politics and Public Affairs in 1999. The annual lecture is made possible by an endowment by Mrs. Crichton.

Dr. Ron Calgaard welcomes distinguished journalist Bill Moyers to the Trinity University Distinguished Lecture Series, started by the university in 1982 to enrich the cultural and intellectual environment on campus and in the community.

young age. I wasn't quite 42 when I became president of Trinity.

But eventually, you reach the point where you say, "I've attended enough commencements and given enough speeches. It's time for someone else to come and provide new energy and put forth a slightly different vision for the institution."

My first retirement has given me six or seven years to do some things I've wanted to do in the community, so now I'm retiring again, and the timing is good. I retired on the 31st day of January as chairman and director of Austin, Calvert & Flavin, Inc. For the first time since I left graduate school in 1963, I'm unemployed.

I am still chairman of the Ray Ellison Grandchildren Trust. I also serve on the board of Valero Energy and as a director of The Trust Company. So I intend to remain fairly active in a business sense, but I'll do it without being on somebody's payroll. My plan is to go to the office a little later, leave a little earlier, and to be gone a lot. My wife and I want to travel, not for months at a time, but simply to be able to pick up on a whim and go somewhere. With my schedule, I've never had the opportunity to do that before.

In fact, your first retirement hasn't been a retirement at all. Over the past several years, you've been chairman, CEO or on the board for numerous investment companies, businesses and civic organizations.

I have been, and this is a time for me to try to reduce the number of places I serve on the board. I've had lots of opportunities to be involved. I've been on the United Way board for 26 years. United Way is forever! But it's been one of the best learning experiences. The United Way has been a vehicle for me to learn a lot of things about San Antonio that I would never have known otherwise.

As an economist by training, you must have a special appreciation for San Antonio's increasingly strong economy.

One area that continues to grow is the health care and biotech sector.

Without question, this is the best of times in San Antonio. While there are still challenges, the economy is increasingly diverse. San Antonio is more visible, more prosperous, and its prospects for the future are better today than they've ever been.

Health care and biotech are leading contributors to the city's booming economy, even when it comes to the military. With plans for Fort Sam Houston to be the head of military medicine in the United States, positions are coming to Fort Sam that are high income, high quality and highly professional. This gives San Antonio another area of visibility, and it adds significantly to our overall quality of biomedical and health care resources.

How do you see SFBR fitting into this?

I think some of the Foundation's greatest potential is in joint endeavors with other local institutions. I believe there are great opportunities for collaboration, and Dr. Tony Infante is in an excellent position to be able to promote these relationships.

There is no question that the chimpanzee and baboon populations at the Foundation are incredible resources for research, as are the genetic resources, the BSL-4 lab, and other outstanding assets. These provide a fantastic advantage, both for the Foundation's own scientists and for their ability to build relationships with others [outside SFBR] who could benefit from their use.

I believe the Foundation has a bright future, with more opportunities ahead. The leadership is excellent and the potential is great over the next five to 10 years for making real progress in biomedical research. I look forward to breakthrough findings that will have a major impact on people's lives.

The "I" in science:

Dr. Pemmaraju N. Rao shares SFBR history of progress through exploration

With 47 years at SFBR, Dr. P.N. Rao is a vital part of the Foundation's history and future.

Throughout your 47 years at SFBR, you've led a distinguished career as an organic chemist, developing novel steroid hormone compounds and innovative diagnostic technologies resulting in 12 patents and 3 pending patents. More importantly, you've impacted physicians' abilities to diagnose and treat reproductive disorders and various cancers. What has been most thrilling for you?

Fortunately, I've always worked in a field that fascinates me, but especially exciting right now is our [group's] recent research, particularly with progesterone receptor modulators. Progesterone is a female hormone that plays a major role in reproduction and other endocrine needs of the female. While it is needed to maintain a healthy pregnancy, it also supports the development of some cancerous tumors.

Our lab has developed some novel steroid hormones called anti-progestins that block progesterone action on these [cancerous] cells, so they could be useful in controlling or reversing the growth of certain tumors. Initial tests have been impressive, and now Zonagen, a company in Houston, is conducting clinical [human] trials on their usefulness in treating endometriosis and shrinking fibroid tumors without surgery.

Haven't you had similar success with other compounds that you originally developed in hopes of treating high cholesterol?

That story goes back to the 1960s, when I worked with Drs. Nicholas Werthessen, Leonard Axelrod and Joseph Goldzieher investigating the role of cholesterol in atherosclerosis (hardening of the arteries). We encountered an estrogen metabolite called 2-methoxyestradiol (2-ME2), which we thought might play a role in lowering cholesterol. I developed some novel derivatives of 2-ME2 for further testing, and sure enough, they were very successful as cholesterol-lowering agents. However, they still had a slight amount of estrogenicity, so people were hesitant to use them for that purpose.

Years later, another group found 2-ME2 to be a powerful tumor inhibitor. It is both cytotoxic, meaning it kills cancer cells, and antiangiogenic, meaning it prevents the formation of new blood vessels and blocks the growth of the tumor. So when Dr. Susan Mooberry joined the Foundation with her cancer drug discovery program, we collaborated with her to test our extensive library of 2-ME2 derivates. Her research showed that some of our derivatives were much more potent than the natural metabolite and had a greater advantage in treating breast cancer tumors and prostate cancer cells.

Since then, our lab has developed 30 new 2-ME2

compounds, which are being tested by EntreMed, near Washington D.C. Interesting data is coming from those studies as well.

You are very well known for the diagnostic technologies you've developed. Would you describe some of those efforts and successes?

During the 1970s, we were pioneers in developing a number of highly specific immunoassays for measuring steroid hormones in body fluids. These methods revolutionized hormone analysis, replacing previous techniques that required more than a week of lab work and allowing analyses to be done in about an hour. Today, these methodologies are routinely used in diagnostic laboratories all over the world.

What are some applications of these diagnostic technologies?

Several help diagnose the cause of infertility. For example, one is used to identify testosterone deficiency leading to low sperm count in males, while another is used to determine whether a woman has estrogen or progesterone levels that disrupt proper ovarian function.

We also developed an immunoassay that is used during pregnancy to gauge the viability of the fetus by measuring a hormone called estriol. Abnormal levels of this hormone can indicate potential problems in the developing fetus.

In recent years, there has been debate over hormone-replacement therapy for post-menopausal women. Premarin, a form of estrogen, is routinely given as part of this therapy, but there is fear that it might lead to endometrial or ovarian cancer in women who metabolize the hormone slowly and develop high concentrations of it in the bloodstream. Doctors need an accurate and sensitive method of measuring the circulation of these hormones so they can determine how well their patients are tolerating the therapy and whether it is safe to continue. Some of our technologies are used for this purpose.

When you talk about "our research," you're referring to a loyal group of people working in your lab, aren't you?

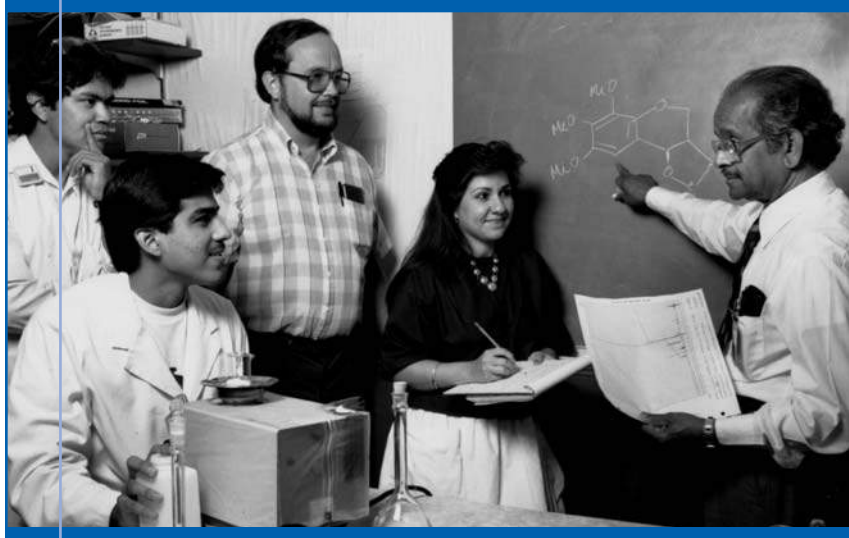
I have a highly talented, stable team. Jim Cessac has been with me for more than 25 years, Kirk Acosta for more than 20, and Anne Marie Simmons, Paul Morrison and Martin Bahr more than 10 years each. Three others joined us a few years ago. This group is my great asset. Because of them, I've been able to transfer ideas to reality, and we've gained national recognition as one of the top steroid research centers in the country.

Your group seems to share your commitment to SFBR. You joined the Foundation back in its earliest days and worked with some of its original leading scientists.

In 1954, I was awarded a Fulbright Fellowship at Rochester Medical School in New York, where I worked with

Dr. P.N. Rao first worked with Dr. Leonard Axelrod (right) at the University of Rochester Medical School.

Later, Dr. Axelrod recruited Dr. Rao to the Foundation, where together they led distinguished careers in science.



Dr. Rao works with postdoctoral associates – his first lab team – in the 1960s.

Dr. Leonard Axelrod. Afterwards, I returned to India, and Dr. Axelrod came to Southwest Foundation. He joined Dr. Nicholas Werthessen, a physiologist, who had found evidence that baboons develop atherosclerosis similar to humans. That prompted the Foundation's research with baboons, and Dr. Werthessen began investigations on the role of cholesterol in atherosclerosis and things of that nature.

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Dr. P.N. Rao believes his dedicated laboratory team is his greatest asset.

Dr. Rao, continued from page 21

Dr. Axelrod did all the steroid biochemistry work, and Dr. Joseph Goldzieher, an endocrinologist, came on board to study steroid hormones. It was a collaborative group, with each one contributing a certain aspect of expertise, but they needed a chemist who could identify and create molecules that had a role in their studies. Dr. Axelrod remembered my abilities from our time in Rochester and asked me to join the group.

One of my first assignments was to make a common chemical called acetic acid labeled with carbon 14, a radioactive compound. When this radioactive acetic acid is injected into baboons, it is converted to cholesterol in the body. This allowed the research team to identify the radioactive cholesterol in different tissues of the baboon, including the fatty plaques of the aorta, and observe how atherosclerosis is formed.

I understand that the Foundation didn't make a great first impression on you.

When I arrived in October of 1958, I was literally shocked to see the facility. Our laboratory was in a shack, or a little barn, really, on the old campus near Callaghan and Ingram roads. One of just three small buildings on campus, it was quite different from the beautiful facilities at Rochester and not at all what I expected. But they assured me we would be moving into new facilities, which we did in 1961. Although the original facilities were primitive, the research was very exciting, so I was happy to be here.

When you arrived, SFBR founder Tom Slick was still alive and involved at the Foundation. How much interaction did you have with him?

Tom Slick was happy about the group Dr. Werthessen had assembled, and he was excited about our studies. So once a month, we met him at The Argyle to discuss our research. But even at the Foundation, he did not sit in a chair and command. He was curious, and very nice, and he would visit the scientists in their labs to learn about their day-to-day activities. He always asked a lot of questions to try to satisfy his curiosity.

Your discussions with him went beyond your research, didn't they?

Yes, I was introduced to Tom Slick as a new scientist from India, which he had visited a couple of times as part of his explorations in Nepal. He used to ask me all kinds of interesting questions about India, including his observations of people who cured poisonous snakebites by chanting some words and antagonizing the venom.

We discussed this at the Mind Science Foundation, which he founded to scientifically explore phenomena of the mind. He assembled some interesting people, and I was curious about their efforts to understand extrasensory perception.

He also was intrigued by the belief in reincarnation and wanted to see if it could be proven scientifically. The scientists conducted some age-regression experiments, using hypnosis to take people back to pre-natal times and get them to talk about a previous life. The idea was to follow up and investigate

whether the person they described actually ever lived. I attended one of these experiments, which Tom Slick also observed.

Today, the organization sponsors things that are more rational, and I have resumed my involvement. The current focus is on finding meaningful answers in the area of consciousness. How does the mind function? What is consciousness? What is the role of the mind in consciousness? These are some of the things they are trying to find out.

What is your involvement with the Mind Science Foundation today?

I am on its board and serve on the research committee. Trying to fulfill Tom Slick's wishes, the group sponsors several competitive research grants to universities and top-notch scientists exploring the human mind.

I also attend the Distinguished Scientist Speaker Series. This involvement helps me intellectualize my curiosity and satisfy my own need to "see what it's all about."

Don't you have a number of other creative interests outside the Foundation? Rumor has it that you're a skilled photographer.

My hobby is photography, and I enjoy it in a creative way by trying to capture things as I really see them. That is why nature and people are my favorite subjects. Nature has so many rich opportunities, and people are fascinating. If a person is really expressing a feeling in his or her face, I want to capture that feeling.

My other love is travel. I try to understand other cultures and see their similarities and differences. Travel is the best education you can get, especially when you go outside the big cities and explore the small towns and countryside to see how people truly live.

I also enjoy organic gardening, and I will never miss a few minutes of meditation each day. That is how I relax my mind and get inspiration for new ideas. I used to do yoga, which my wife has taught for the Northside School District's continuing education department for many years. I believe yoga and meditation help you attain good health.

Aren't you and your wife involved in a number of other community activities, particularly with the local Indian community?

Yes, my wife helps the Indian community with public relations work, and I was formerly on the board of the Hindu Temple of San Antonio. I also serve as an advisory trustee to the Witte Museum, and I am a trustee on the Carver Development Board.

None of your children followed in your footsteps to become a scientist, but you must be very proud of what they're doing today.

Certainly. My daughter, Uma Pemmaraju, has been interested in journalism since middle school. Today, she works as an anchor for Fox News. Both of my sons are medical doctors working in Dallas. Rama specializes in internal medicine and child psychiatry, and Sankar specializes in physical medicine and rehab.

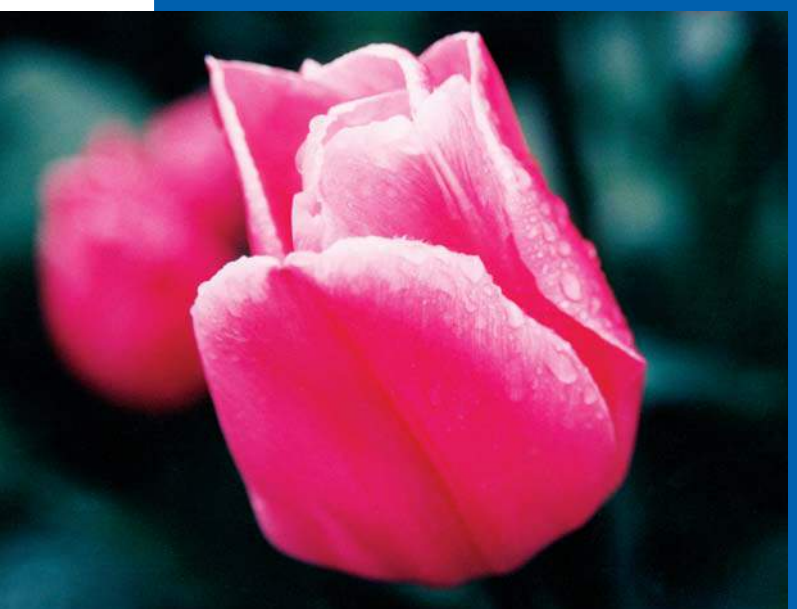
My children told me they didn't want to become scientists because of the competition we face and the struggle we go through in getting research grants. They all work in demanding fields, but they wonder how I've survived having to compete for grant renewals or new funding every few years.

Has the struggle for research funding ever discouraged you?

I'll tell you, a scientist's life is not easy. You have to have a good idea, and you have to have an idea that can get funded. But that is a challenge I've enjoyed, and fortunately, things have worked out. I've had consistent funding from the National Institutes of Health, the World Health Organization, the FDA, and private industry.

Life is about overcoming challenges, and I enjoy my work. It is like a hobby for me, because it is one of the aspects of my life that gives me joy. As long as I see it that way, it is something I plan to continue.

Dr. Rao's love for travel, photography and nature combine in this photo of a tulip, which he took during a trip to Holland.



In order to learn more about different cultures, Dr. Rao and his wife like to get off the beaten path and explore the countryside when they travel, as shown in this photo of their trip to Peru.

Joining SFBR's mission to

improve human health

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

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

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

The Golden Circle

Members of the Golden Circle, Benefactor Circle, President's Circle, and Chairman's Circle are among SFBR's closest friends and supporters. Each year, they make contributions of $10,000, $5,000, $2,500 and $1,000, respectively, to assist SFBR in carrying out its mission. These donations are used by the Foundation to purchase new scientific equipment and other resources necessary to its life-saving research projects.

To thank our partners in progress for their generosity, SFBR typically hosts two special events during the year in their honor. Just before the holidays, on Nov. 14, they gathered at The Argyle for a reception and dinner featuring a presentation by Dr. Anthony Infante. As the new president of SFBR, Dr. Infante wanted to update these valued friends on the Foundation's current progress, explain what he sees as its greatest strengths, and outline his vision for leading the organization to even higher levels of achievement.

The evening was a true celebration of SFBR's history of progress and its future aims for breakthrough scientific findings that improve human health. Some memorable photos from the evening are provided on the following page.

If you would like to become a partner in scientific progress through membership in the Golden Circle, fill out and return the form provided on page 26, 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.

An evening with Dr. Infante, ushering in a new leadership and vision…

Golden Celebration

Going beyond the expected
to impact the future

by B. Corbett Christie, *Chief Development Officer*

"If you want to innovate, to change an enterprise or a society, it takes people willing to do what's not expected."

– Jean Riboud

Who would have expected, in 1941, that the selfless action of the visionary 25-year-old Tom Slick would lead to the creation of what is today one of the leading independent biomedical research institutions in the United States? Tom Slick did.

Today, SFBR prides itself on being an important part of the research and technology community in this region as well as the world. However, this never would have happened without the visionary founding of this organization by Tom Slick, who was willing to venture well beyond the expected to fulfill a dream. Nor would it have happened without the legion of philanthropic supporters who have supported the organization ever since. They, too, have been willing to do the unexpected, helping build and staff the laboratories that make SFBR's success possible. Indeed, for SFBR, "the unexpected" has led to exceptional results.

Scientific innovation and the quest for scientific breakthroughs are at the heart of Southwest Foundation's motivation. Together, through the ingenuity of brilliant researchers, the investment of generations of donors, and the guiding vision of our leadership, we have grown an institution that is dedicated to improving the health of our global community through innovative biomedical research.

Do you have the desire, like Tom Slick, to do what's not expected? Do you want to do something significant to impact the future? Consider these ways to get involved – or expand your involvement – in SFBR.

Become a member of the Golden Circle. Your donation of $1,000 to $10,000 annually helps fund needed innovation, technology and pilot research at SFBR. Members of the prestigious societies enjoy educational, social and travel opportunities reserved for members only.

Become a member of the Southwest Foundation Forum. The Forum welcomes women (over the age of 21) who are interested in promoting the life-saving work of SFBR. Forum members serve as ambassadors as well as fundraisers for SFBR by sponsoring a spectacular gala annually to fund pilot research, offering lecture luncheons about scientific research, hosting high school student tours of SFBR, and awarding science grants to area high schools, among other activities.

Become a member of the Founder's Council. This "get-involved" group of young community leaders sponsors lecture luncheons and social activities to inform the community about SFBR, while membership donations provide funds for the purchase of laboratory equipment by SFBR scientists.

Remember Southwest Foundation in your will. Many donors choose to include a specific or general bequest through their will or codicil.

Establish an endowment to support life-saving research at SFBR. Endowment is a perpetual source of annual support for research. You determine the purpose of your endowment and can be assured an impact long after your life.

Establish a life income gift to SFBR. This gift can pay income to you as long as you live and then benefit SFBR upon your death.

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

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

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

Please check the appropriate box:

☐ **Golden Circle,** unrestricted contributions of $1,000 or more to directly support indispensable biomedical research.

☐ **Benefactor Circle,** unrestricted contributions of $2,500 or more which also fund vital biomedical research.

☐ **President's Circle,** contributions of $5,000 or more to directly support the growing need for state-of-the-art equipment.

☐ **Chairman's Circle,** contributions of $10,000 or more to fund strategic initiatives that require immediate investment at the discretion of the Chairman and Board of Trustees.

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

Dr./Mr./Mrs./Ms.
Name

Spouse's Name

Home Address ☐ Check if preferred mailing address

City State Zip

Home Phone Business Phone

E-mail

Business Title

Company or Foundation Name

Business Address ☐ Check if preferred mailing address

City State Zip

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

☐ MasterCard ☐ Visa ☐ American Express ☐ Discover

Card # Exp. Date

Name on Card

Billing Address

City State Zip

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

My annual membership in the amount of $_____ is enclosed. Please make your check payable to SFBR. Your contribution is tax deductible.

Southwest Foundation Forum

On a fun-filled race in support of science

The Southwest Foundation Forum has chosen "Run for the Roses" as the theme for its 2006 Gala, but truth be told, this dedicated group of women has been off and running all year long.

With a strong focus on education, the Forum hosted a sell-out Fall Lecture Luncheon at The Argyle on Nov. 16. There, Dr. Lorena Havill outlined her research on osteoporosis, or fragile bone disease. As Dr. Havill explained her search for genes that will make good targets for prevention and treatment, she also offered advice on healthful lifestyle habits to help prevent this debilitating disorder.

On March 22, Forum members gathered for the Spring Lecture Luncheon, which featured SFBR President Dr. Anthony Infante and his vision for the Foundation's future. Special guests included representatives of local high schools receiving this year's Science Education Awards, granted by the Forum in conjunction with the V.H. McNutt Memorial Foundation. Totaling $14,000, the grants will be used to support innovative science projects at these winning schools: George W. Brackenridge High School, first place; Health Careers High School, second place; Cibolo Alternative Program, third place; Tom C. Clark High School, fourth place; and Byron P. Steele II High School, fifth place.

Thanks also go to the L.D. Ormsby Foundation for contributions made to each school that applied for one of these awards.

Ten other local high schools benefited from a series of Forum-sponsored SFBR tours from January through March, all meant to encourage the bright young minds of today to consider scientific careers in the future.

'Run for the Roses' with the 2006 Gala

The Forum's annual gala is both a premier social event and an outstanding fundraiser for biomedical research at SFBR. The 2006 Gala, slated for May 6 in conjunction with the 132nd Kentucky Derby, promises to "transport guests to a night of southern splendor, racehorse style!" said Gala Co-chair Caroline Schupbach. Although this popular event often sells out well in advance, opportunities for involvement are still available. Anne Johnston, who is handling individual reservations, also is selling tickets to the gala's first-ever "After Party," which begins at 9:00 p.m. and offers drinks, games and dancing. She can be reached at 210-826-2305.

Raffle tickets for extravagant prize packages also are available for purchase in advance or at the event, and volunteers are always needed to help with event set-up. For either opportunity, contact Gala Chair Estee Kellogg at 210-822-7574.

Mrs. Kellogg extends her appreciation to the event's generous sponsors, including lead sponsors AT&T, the Mays Family Foundation, and Valero Energy Corp. Special thanks also go to Tiffany & Co., a generous sponsor of both SFBR and the Forum, which is providing beautiful party favors for gala guests.

For membership and other Forum information, visit the group's Web site at www.swff.org.

Forum members enjoy time to mingle before recent lecture luncheons at The Argyle.

The Founder's Council

Participating in the future of SFBR

As Matthew Bell, the new president of the Founder's Council, shared his personal excitement about leading the group in support SFBR, he welcomed members to a luncheon with the man at SFBR's helm: Dr. Anthony Infante. The Foundation president served as the group's featured speaker on Feb. 22, offering candid information about himself, SFBR's contributions to science and the local economy, and his vision for SFBR's future achievement. Sponsored by DPT Laboratories, the luncheon was a perfect follow-up to the group's Holiday Party in December, when they made their own mark on the Foundation's future.

Held at the lovely Tobin Estate and co-sponsored by the Tobin Endowment and PacifiCare of Texas, the Holiday Party was an evening of celebration. The Council thanked retiring board members, welcomed new ones, and awarded more than $23,000 in grants to SFBR scientists for the purchase of research equipment.

The Steves Grant, awarded in honor of the late Albert Steves IV, went to Dr. Charles Criscione for the purchase of a microscope used in research on schistosomiasis.

Other grants went to Dr. Jean Patterson for an instrument that amplifies millions of copies of DNA for research on Ebola and Marburg viruses, avian flu, anthrax, and bubonic plague; Dr. Tim Anderson for a device that provides rapid measurement of DNA for his research on malaria; Dr. Tony Comuzzie for a device that measures physiological parameters associated with obesity, diabetes and other metabolic diseases; Dr. Kathleen Brasky, for an instrument that provides intraocular pressure readings useful in eye-trauma cases as well as the diagnosis of glaucoma and ocular hypertension; and Dr. Qiang Shi for supplies necessary to his investigations on atherosclerosis.

Some special guests added to the festive yet intimate feel of the evening. Council founders Bruce Bugg and Jim Gorman were in attendance, as was Leroy Denman, a co-trustee of the Tobin Estate and the attorney and personal friend of SFBR founder Tom Slick. Mr. Denman also is a founding trustee of SFBR.

In addition, a niece of Tom Slick, Catherine Nixon Cooke, attended the reception and shared compelling stories about her uncle's life from her new biographical book, *Tom Slick: Mystery Hunter*. The stories were an inspiration to all who aspire to follow in his footsteps by being visionaries who work for the betterment of humankind.

The Founder's Council is kicking off its membership drive for 2006-2007 as it gears up for its May 17 event: a "virtual tour of SFBR." At this cocktail reception, participants will make their way around The Argyle to visit with several SFBR scientists sharing video presentations and personal discussions about their innovative research.

For more information about upcoming events or Founder's Council membership, contact Amy Abdalla at 210-258-9409 or amy@sfbr.org, or log onto www.sfbr.org/pages/founder_council.php.

Enjoying the Feb. 22 luncheon are representatives of DPT Laboratories, the event's sponsor.

On hand for the Holiday Party were council founders Bruce Bugg and Jim Gorman, Tom Slick's niece Catherine Nixon Cooke, and SFBR founding trustee Leroy Denman.

Francie Steves Calgaard and Martha Steves with Steves Grant recipient Dr. Charles Criscione.

Matthew Bell and Kevin Kennedy (back) with SFBR grant recipients.

SFBR campus renovations

Touring the construction site of the new Denman Atrium on the SFBR campus are Dr. Greg Patterson, SFBR associate scientific director; Bruce Bugg, co-trustee of the Tobin Endowment; Dr. Anthony Infante, SFBR president; Corbett Christie, SFBR's chief development officer; and Leroy Denman. Mr. Denman has a long history with SFBR, having been the personal friend and attorney of SFBR founder Tom Slick, as well as a founding trustee of the organization. During the Foundation's recent capital campaign, the Tobin Endowment donated funds for the new Denman Atrium, currently under construction as part of laboratory and office renovations on the SFBR campus.

Southwest Foundation for Biomedical Research

Donation Form

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

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

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

My donation is for:

_____ **Memorial**
In memory of _____

_____ **Special Occasion** (Please list occasion and honoree.)
In honor of _____

_____ **General Contribution**

Name to be listed as the donor:

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

Send an acknowledgement card to:

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

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

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

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

To make a donation online, go to www.sfbr.org and click on "Support SFBR/Make a Contribution"

About Southwest Foundation

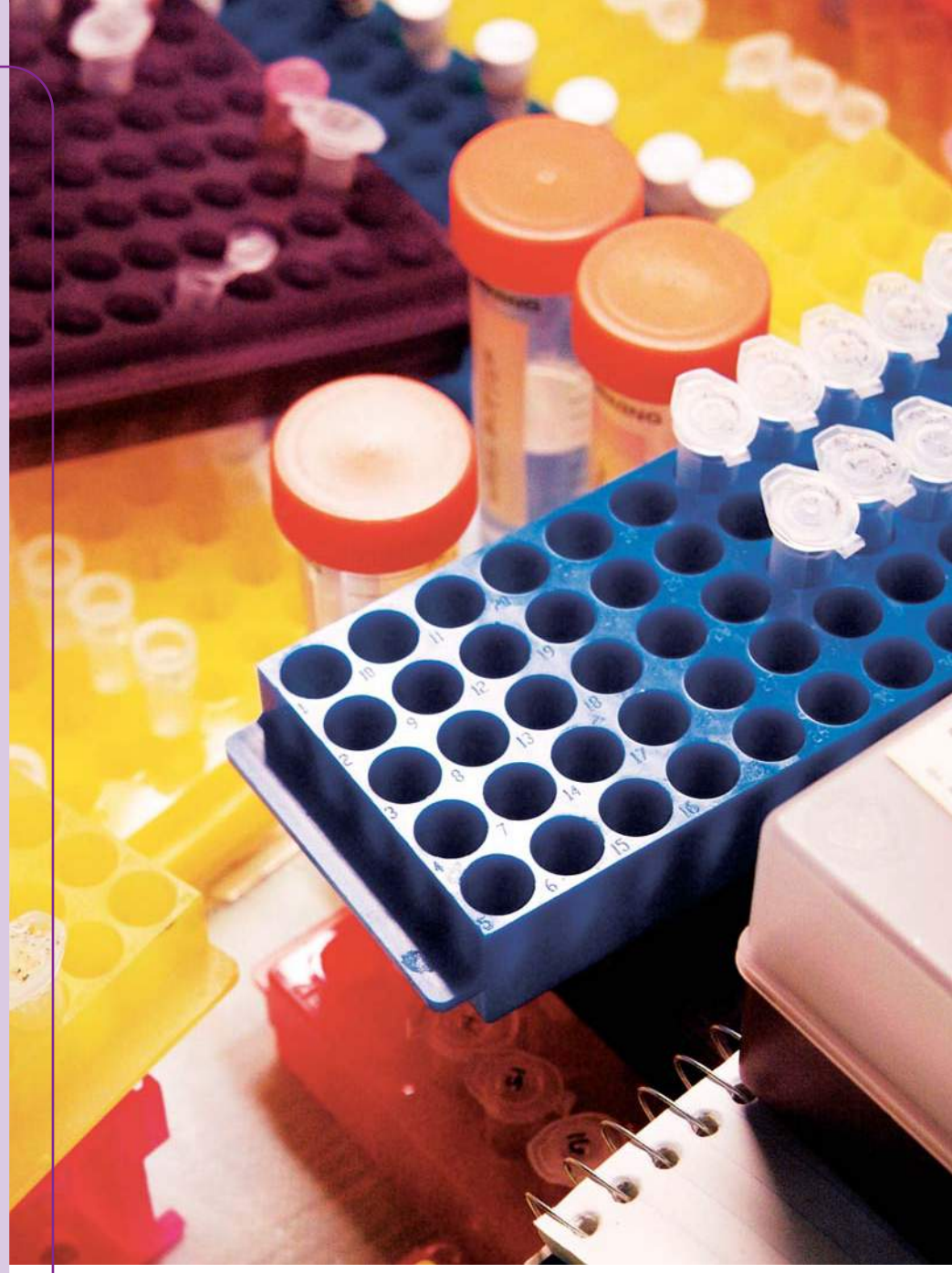
As one of the world's leading independent biomedical research institutions, the Southwest Foundation for Biomedical Research is advancing human health. Today, SFBR's multidisciplinary team of nearly 75 doctoral-level scientists work together on more than 175 major research projects.

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

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

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

Southwest Foundation for Biomedical Research is dedicated to advancing the health of our global community through innovative biomedical research. For more information, please contact the Foundation at 210-258-9400, or visit our website, www.sfbr.org.



PROGRESS

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