

# Progress

in Biomedical Research

A Publication of the Southwest Foundation for Biomedical Research

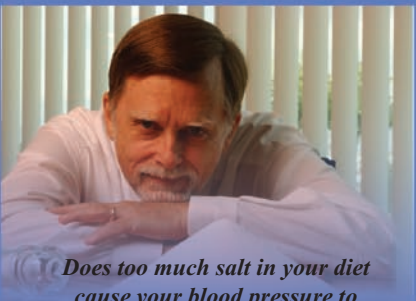
Summer 2002

## Gene Crunching for Medical Breakthroughs



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**Dr. Frank  
Ledford**  
*President*

**PRESIDENT’S COLUMN**

At the Southwest Foundation for Biomedical Research, we are in a time of unparalleled excitement and growth toward the future. Our campus is in the midst of a \$40.3 million modernization campaign, and our scientists are making great strides in their research.

This issue of the newly redesigned *Progress in Biomedical Research* highlights just a few of the tremendous activities we have going on at our campus. I’m pleased to share them with you, and encourage you to learn more about our science.

Our cover story features the SBC Genomics Computing Center that will open on our campus in early 2003. This really is the story of a leading company in telecommunications joining forces with a leader in genetic research. On behalf of our Board of Trustees and scientists, we are grateful to the SBC Foundation for making this high-performance computing center a reality. What it will mean to our scientists in their search for the genes influencing common complex diseases is incredible. What now take two days of computing time will take just three minutes. Genetics is the new frontier in science, and we are proud to be major participants in that scientific exploration.

You’ll read how our geneticists are exploring the world to find the best ways to study the role of genes in human disease. From Nepal to Brazil, our scientists are conducting research with worldwide impact. At home, our large genetic research project with the Mexican American population is charting new paths in looking for the genes that contribute to heart disease and its associated risk factors. Diabetes and obesity weigh heavy in our city, diminishing the quality of life for so many individuals.

Speaking of San Antonio, our thanks to Mr. Red McCombs for being the first member of our Board of Trustees to go “*In the Spotlight*.” Mr. McCombs has been a most valued member of our board since 1979, and we’re delighted to share some of his insights.

Red’s “deep respect and admiration” for the researchers at the Foundation is shared by so many of us that we thought it would be interesting to reveal a more personal side of our scientists in each issue of *Progress*. This issue’s profile is on Dr. John Blangero, who recently received one of the most prestigious awards in science, a MERIT Award from the NIH. Our congratulations to Dr. Blangero on this most impressive feat, and our thanks to him for choosing the scientific spotlight rather than the rock ‘n’ roll stage.

SFBR’s scientific director, Dr. Robert Shade, is one of the pre-eminent physiologists in the world for his studies on hypertension. As a physician, I can tell you the dangerous role hypertension plays in contributing to our nation’s leading killer, cardiovascular disease. Dr. Shade’s collaboration with the UT Health Science Center at San Antonio will help scientists uncover the mysteries behind salt’s effect on blood pressure regulation.

I hope you will join us in our excitement over what is happening at Southwest Foundation, and thank you for your valuable support of our 60-year-old organization.

**Southwest Foundation’s New Look**

Just as the campus for the Southwest Foundation for Biomedical Research is undergoing an extensive modernization, so too is the Foundation’s institutional identity. Southwest Foundation’s logo has been updated with a new look that emphasizes the initials “*SFBR*.” This simplified moniker should provide our constituents with an easy but distinctive reference for the Foundation and enhance our name recognition within the community.



**SFBR Factoids**

The first baboons that Southwest Foundation imported from Africa were originally housed at Oakwell Farms by Mrs. Margaret Tobin.



The scientist with the longest tenure at SFBR is Dr. Pemmaraju N. Rao, an esteemed organic chemist who joined Southwest Foundation in 1958.

As a community service, SFBR’s seven practicing veterinarians donate time to provide requested medical care and consultations for various animal sanctuaries and veterinary offices in the San Antonio area. In addition, several SFBR scientists have used their own time to create Chimp Haven, Inc., a corporation to build and operate a 200-acre sanctuary near Shreveport, La., for chimpanzees previously used in research.



Southwest Foundation’s operating budget has grown from \$23.6 million in 1996 to a projected \$48.8 million in 2002. This will generate an economic impact on the local community of approximately \$150 million.

SFBR expects to complete \$25 million worth of construction projects on its 332-acre campus in the next three years.



Last year, Southwest Foundation scientists were awarded more than \$35 million in new grants and contracts. It was the Foundation’s sixth consecutive year of increased awards.

**About Southwest Foundation**

As one of the world’s leading nonprofit independent biomedical research institutions, the Southwest Foundation for Biomedical Research is advancing human health. Today, SFBR’s multidisciplinary teams of 66 doctoral-level scientists work together on 177 ongoing 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 coronary heart disease, diabetes, obesity, cancer, hypertension, psychiatric disorders, AIDS, hepatitis, malaria, parasitic infections and a host of other infectious diseases.

Southwest Foundation is the site of the Southwest National Primate Research Center and home of 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 and contracts. Remaining expenses are met by the generous contributions of foundations, corporations and individuals, as well as earnings from SFBR’s permanent endowment.

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

**Credits**

*Progress in Biomedical Research*, a quarterly publication of the Southwest Foundation for Biomedical Research, is produced by Riccelli Creative, with concept, design and layout by Richard G. Klaver and writing by Christiane L. Dahl, APR. Photography is by Clem Spalding, Geno Loro, Jr., Joan Snow and Southwest Foundation.





## In the Spotlight:

# Red McCombs

*Why did you decide to sign on as a member of Southwest Foundation's Board of Trustees? What do you think of the team?*

I was impressed with the work of Southwest Foundation from the time I first heard of it and thought it an honor to be asked to join the Board of Trustees.

I consider the Foundation a true treasure, and I look at my role as a trustee as being one that is a deeply felt responsibility. I think the more San Antonio becomes aware of the mission of Tom Slick and what's been carried on there in the 60 years since he founded the institution, the more the Foundation will be considered a treasure by everyone.

I think we have a great team. The experience of the people on the Foundation board is well complemented by the new members who come aboard with fresh ideas. The leadership has been excellent. I'm on a lot of boards, and this is one of the best I've ever been on.

In the league of research institutions, we compete very well. That's obvious by the tremendous research funding we receive. The Foundation's research truly has been outstanding.

*In looking at research as a football game, what kind of scores would you like to see the Foundation make? A Hail Mary pass such as an instant cure for AIDS or a long drive down the field, churning out the small-step discoveries that are the building blocks of science?*

What I'd like to see is what they are doing already. I have the greatest respect for researchers who can conduct a daily search for all of the answers, despite the fact that they have no promise of success. It's the inquisitive, intelligent aspect to their work that I find fascinating. So many positive things come out of the Foundation that it's a great feeling of progress for those of us who are philanthropists of gifts and time to the board. The researchers seem to have no end to their creative imaginations in areas they are studying, whether it's hepatitis or diabetes. To make improvements in even a tiny way in any of these diseases is really a home run.

*If you were drafting for the Foundation, what types of players would you pursue? Would you look for the superstar from a Big 12 school or for the promising unknown from the Mid-Atlantic Conference?*

What you are looking for in drafting for your team are people who make a positive contribution toward being the best. You search for those talents. At the Foundation, you look for this same quality as you do for a sports team. I think the Foundation has been given very good grades on the people it has selected.

Small schools, large schools. Our God really didn't put geographical or other parameters around inquisitive, bright minds. I think the staff as well as the board of the Foundation finds a great strength from the vision Tom Slick had in creating the Foundation and setting its goals. I feel a sense of that in all of the opportunities out there.

*If you were calling a surprise play, what would one be that your fellow Board of Trustee members would never suspect? What would they be surprised to learn about you?*

I think one of the things they would be surprised about is the deep respect and admiration I have for the people who do the research. Most of the things I'm involved in have an obvious "win or loss" tag. To do what the scientists do daily — through dogged determination — to stay the course and stay so strongly motivated by it, has made a deep impression on me.

*The Minnesota Vikings want a new stadium. Southwest Foundation needs a modernized campus. As a Board of Trustee player, why do you feel it is important to modernize the campus, and for the community to support this modernization?*

To perform at their maximum opportunity, this is a real component for success. We could both still play the game without new facilities, but neither would perform at its maximum level without them. I'm not sure that winning NFL football games is in the same league as winning in the research lab, but they both require all the tools possible for excellence.

The modernization plan put forward by the Board of Trustees in the 1990s speaks to the vision of Tom Slick. Tom Slick left us with a lot of acreage — a very good footprint to work from.

*How would you increase the fan base of Southwest Foundation? We have The Argyle as our VIP suite, but how would you go about filling the "nosebleed" seats? Why should everyone be a fan of biomedical research?*

It's very important that everyone in a leadership role with Southwest Foundation do better at expounding on what a great product the Foundation is. We have a story that is very positive. All of us on the board can look at doing a better job of telling the story.

There are hundreds of thousands of people who pass by the Foundation grounds. Not nearly enough of them have any real concept of what goes on there. That is a role all of us on the board should take on as a challenge.



Continued on page 16





**The SBC Genomics Computing Center  
will open in early 2003**

What makes individuals susceptible to common complex diseases such as heart disease, diabetes, obesity, osteoporosis, infectious diseases, thrombosis, Alzheimer’s disease and psychiatric diseases?

Why is it that some individuals who strictly adhere to all the heart-healthy guidelines still get cardiovascular disease, while others who smoke and never exercise live well into their nineties?

Scientists have proven there is more to physical and emotional well-being than unhealthy lifestyle choices or environmental factors. Differences in genetic makeup help determine why some people get certain diseases and others don’t. Truly, the study of the role genes play in human health has become the new frontier in science. The recent development of the human genome map has paved the way for unparalleled scientific exploration. That remarkable exploration is happening today at Southwest Foundation.

Through their unique capabilities and resources, Southwest Foundation scientists are conducting landmark genetic research into finding and identifying individual genes that influence risk of common complex diseases. Southwest Foundation

geneticists already have detected 38 genes that contribute susceptibility to common diseases and their risk factors.

**FINDING ANSWERS FOR THE MEDICAL  
BREAKTHROUGHS OF TOMORROW**

Genotype is the internally coded, inheritable information carried by all individuals that serves as a “blueprint” for building and maintaining the body. Because the relationship between genotype and disease risk is complex, researchers in SFBR’s Department of Genetics have developed revolutionary statistical methods for locating where disease genes are found in the human genome.

Led by Dr. John Blangero, Southwest Foundation’s statistical genetics group is acknowledged as an international leader in methods for analyzing common disease genetics. His group uses novel mathematical/computational methods that take advantage of genetic information inherent in large extended families, as opposed to the more conventional use of siblings or nuclear families.

**Gene Crunching for Medical  
Breakthroughs**

Dr. Blangero’s group has developed a computer software package, SOLAR (Sequential Oligogenic Linkage Analysis Routines), that is used by researchers all over the world to analyze data obtained from large families in which diseases appear to be inherited. The SOLAR software has been used to locate genes influencing disorders such as obesity, diabetes, heart disease, thrombosis, infectious disease, osteoporosis and depression.

At SFBR, this statistical genetic analysis software has been adapted to use an impressive parallel computing network that includes several hundred fast computer processors. The computer and file server hardware consists of Sun Microsystems SPARC processors connected to Sun workstations and desktop

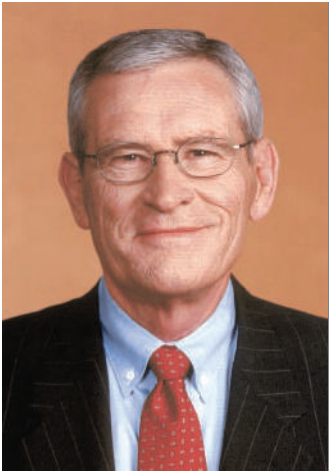
computers. Under the direction of Dr. Bennett Dyke, this technology proved to be so successful that the computer “ranch” became the Foundation’s major computing resource for large-scale analysis.

Since 1996, the ranch has gone through several expansions and upgrades. Today, however, it has outgrown its current location on the Foundation campus, turning it into a limiting factor in producing rapid breakthroughs in Southwest Foundation’s research on complex human diseases.

**A WORLD LEADER IN TELECOMMUNICATIONS  
SUPPORTS A WORLD LEADER IN GENETIC RESEARCH:  
THE SBC GENOMICS COMPUTING CENTER**

The SBC Foundation, which is the charitable giving arm of San Antonio-based SBC Communications Inc., recognized the need for a new center at SFBR that was dedicated exclusively to high-performance genomics computing.

In the spring of 2002, the SBC Foundation stepped in with a major grant to make the center a reality. SBC admired Southwest Foundation’s creative use of technology to solve real human problems, and as a technology company, naturally gravitated toward supporting this type of project.



*“The SBC Genomics Computing Center  
will dramatically improve the ability of scientists at the  
Southwest Foundation for Biomedical Research  
to identify genes influencing common diseases such as  
heart disease, osteoporosis, diabetes and more.  
We are very proud to support this important work.”*

— Ed Whitacre  
Chairman and CEO  
SBC Communications Inc.



“The SBC Genomics Computing Center will dramatically improve the ability of scientists at the Southwest Foundation for Biomedical Research to identify genes influencing common diseases such as heart disease, osteoporosis, diabetes and more,” says Ed Whitacre, chairman of SBC Communications Inc. “We are very proud to support this important work.”

The attractive 6,741-square-foot center, scheduled to open in early 2003, will be a free-standing building located near the Loop 410 entrance of the Southwest Foundation campus. It will serve as a showcase of the genetics department’s technological capabilities and will be the primary site of statistical genomics research.

“We are generating a huge volume of data, and the speed at which you can get through that data is limited only by the computing resources available,” explains Dr. Sarah Williams-Blangero, chair of the Department of Genetics. “By increasing the computing available, you are increasing the rate at which you can make scientific discoveries using the data that has been generated, and will continue to be generated.”



In the new high-performance computing facility, SFBR scientists will take their research and combine it with the science world’s newly gained human genome sequence information to further develop statistical methods that take advantage of genetic information inherent in large families.

TURNING MONTHS OF COMPUTING TIME INTO DAYS

When it opens next year, the SBC Genomics Computing Center will house the parallel computing resources needed for the full implementation of the novel statistical genetic tools that SFBR scientists have developed during the past decade. Initially, the center’s computer ranch will use 1,000 processors configured in parallel. The center will be easily expandable, with substantial added computing efficiency obtained with each new processor.

“Over the past four years, a tremendous increase in capabilities has been achieved,” Dr. Williams-Blangero says. “Analyses that took two weeks in 1998 when parallel processing was first implemented by SFBR scientists now can be completed in two days. Our goal is to increase our computational speed 1,000-fold with the creation of the SBC Genomics Computing Center. This dramatic change will reduce the time required for our two-day analyses to just three minutes.

“The new SBC Genomics Computing Center will provide an absolutely unique resource, so it greatly enhances our department as an international center for computational genomics research,” Dr. Williams-Blangero says. “In terms of our outside collaborations, it’s viewed as a tremendous resource that other people would like to have access to. It will enhance our ability to pursue collaborations with other academic groups.

“For our own research programs, it will speed up things so much that the time between when we start an analysis and when we get to our product in terms of finding the gene will be decreased tremendously,” Dr. Williams-Blangero adds. “It will be a tremendous benefit to all of the genome scans that we have going on.”

SFBR geneticists are conducting genome scans of some 13,850 individuals in eight populations as they search for genes affecting heart disease, diabetes, obesity, aging, osteoporosis, schizophrenia and parasitic diseases. A total of 5.5 million genotypes are being generated as part of these research efforts.

By placing Southwest Foundation at the cutting edge of genetics research in the 21st century, the SBC Genomics Computing Center will aid in recruiting outstanding new faculty and postdoctoral fellows to the Foundation. The center will enhance the abilities of SFBR individual investigators to generate NIH and industry support for new research projects. This will be a tremendous benefit toward retaining the highly sought-after faculty already working at Southwest Foundation.

*“In our statistical genetics program at Southwest Foundation, we are dedicated to finding and identifying genes that influence risk of common diseases.*

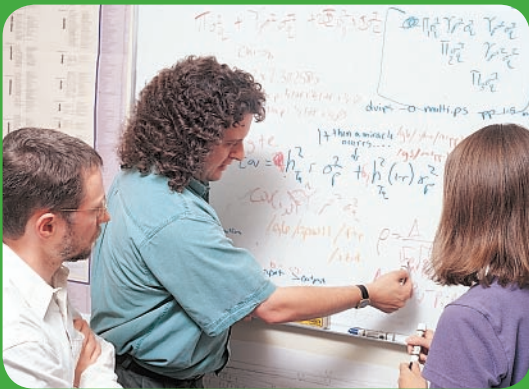
*We find order in chaos! Because the relationship between genotype, as seen in the DNA, and disease risk is complex, all inference in complex disease genetics is statistical. This requires enormous computational resources.*

*We’re acknowledged as world leaders in theory and methods for analyzing common disease genetics. We came up with a solution for a major problem in human genetics. We used novel mathematical/computational methods to allow the analysis of quantitative traits in pedigrees (families) of arbitrary size and complexity.*

*We’ve located genes, we’ve identified genes, and we’ve found the mutational variations in genes that lead to risk for some diseases. However, to put our theory and methods into wide-scale application and apply them to finding the genes for the important diseases that we are working on, it’s going to require massive computing power.*

*We’ve had great results in the past, but now with the new SBC Genomics Computing Center, we’re really going to open up the black box of human genetics. Our greatest scientific successes lie before us.”*

— John Blangero, Ph.D.  
Scientist, Department of Genetics  
Southwest Foundation for Biomedical Research



GENES MAPPED BY SFBR SCIENTISTS

Heart Disease	11 genes
Thrombosis	7 genes
Obesity	6 genes
Psychiatric Diseases	5 genes
Diabetes	4 genes
Osteoporosis	2 genes
Infectious Disease	2 genes
Alzheimer’s Disease	1 gene





A GLOBAL HUNT FOR DISEASE-CAUSING GENES

Southwest Foundation geneticists are on a mission to advance our understanding of the role genes play in determining susceptibility to many international health problems, from heart disease — the leading killer in the United States — to malaria, which kills more people worldwide than any other communicable disease except tuberculosis.

SFBR is known for its innovative research with nonhuman primates, including the development of the baboon gene map. But just as revolutionary is its development of unique large-scale genetic studies in populations throughout the world.

These studies involve large extended families — called “pedigrees” in the scientific arena — with as many as 2,000 individuals for each project. This “strength in numbers” offers tremendous advantages in terms of the power of these projects for finding and ultimately identifying genes influencing many diseases. Additionally, these studies are being expanded into other, smaller-scale projects that are of great importance to human health.

The evidence for disease-susceptibility genes is obtained by statistical genetic analysis of patterns of variation in disease risk factors within families. Large-scale genetic studies are so complicated, however, that they only can be analyzed by using the powerful statistical techniques and parallel processing available at SFBR. The high-performance computing capabilities of the new SBC Genomics Computing Center will greatly speed up the search for genes affecting disease.

“Our research with human populations has expanded rapidly in recent years,” Dr. Williams-Blangero says. “These studies often have an immediate impact on the health of the participants through treatment and/or medical exams that are part of the study protocol, in addition to contributing to the future development of more effective interventions through increasing knowledge of the genes determining disease risk. Thus, elements of health care and research are necessarily intertwined in most of our studies of human families, making these research efforts particularly suited to advancing Southwest Foundation’s mission to improve human health through research.”

FROM THE HILLS OF NEPAL TO RURAL BRAZIL

For their human genetic research on chronic and infectious diseases, Foundation geneticists have developed several major field sites around the world.

The genetics of host susceptibility and response to infectious diseases is one of science’s most exciting frontiers. Just as individuals can inherit genes making them susceptible to obesity, they also can inherit genes that make them vulnerable to infectious diseases. By finding the genes that affect this susceptibility, scientists will be better armed to develop new treatments for infectious diseases. Ultimately, this will facilitate discoveries that could save millions of lives each year.

INTESTINAL WORM INFECTION IN NEPAL

In the Jiri region of the eastern hills of Nepal, Southwest Foundation conducts studies on one of the most powerful human pedigrees available for genetic analysis. The *Jiri Helminth Project* is a long-term study of the genetic determinants of susceptibility to soil-transmitted parasitic worm infections.

Participating in the study are 2,000 members of the Jirel population, a small ethnic minority group which experiences high rates of infection with intestinal worms, including hookworm, roundworm and whipworm.

Dr. Sarah Williams-Blangero and Dr. John Blangero have conducted years of work with the Nepalese population to gain extensive information on family membership in the group. This valuable information allows placement of all 2,000 individuals in the study into a single family pedigree, which is extremely powerful for genetic analysis.

Already, Dr. Williams-Blangero and her colleagues have demonstrated that there are significant genetic influences on susceptibility to infection with the roundworm in the Jirel population. More than a quarter of the world’s population is affected by this parasitic disease, which can cause serious illness and even death.

The data collected from the *Jiri Helminth Project* also are being used for a genome scan to identify the specific genes in humans and in the roundworms themselves that determine susceptibility to helminthic infections. The project focuses on intestinal worm infections that pose a widespread health problem for young children in developing countries.

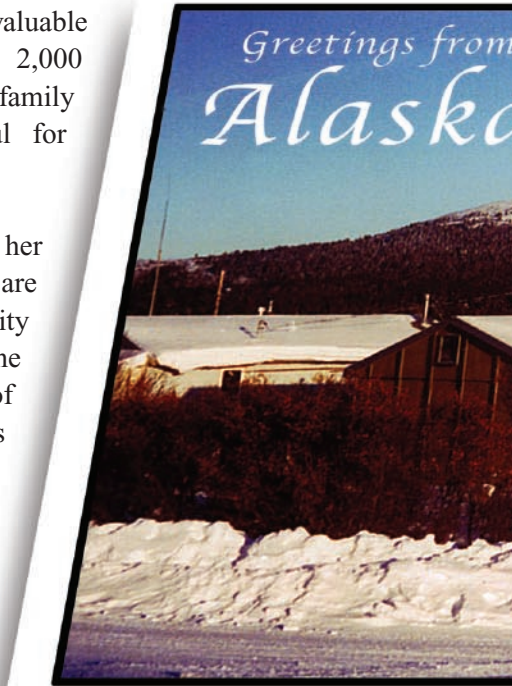
CHAGAS’ DISEASE IN BRAZIL

In the *Posse Family Health Study*, Foundation researchers are studying the genetic determinants of Chagas’ disease, a parasitic disease that is the leading cause of heart disease in Central and South America. Research is focused on a rural population in central Brazil that experiences a high rate of heart disease which results from an infection with the parasite *Trypanosoma cruzi*.

More than 60 percent of the members of the population being studied are infected with the protozoan organism and have, or are at risk of developing, the progressive cardiomyopathy associated with chronic infection and Chagas’ disease. Through the study, SFBR researchers hope that genetic approaches will yield insights into potential new mechanisms for treatment and prevention of this horrible disease.

Led by Dr. Williams-Blangero and Dr. John VandeBerg, a scientist in the Department of Genetics and director of the Southwest National Primate Research Center, the *Posse Family Health Study* seeks to determine what genetic factors are influencing susceptibility to infection with the parasitic cause of the disease and what factors affect progression of the disease after infection.

By gaining knowledge of the genetic mechanisms involved, health professionals will be better able to clinically manage the disease in infected individuals. Ultimately, they may be able to identify new biological pathways to target drug development to more effectively treat the disease.







## FROM THE 'LAST FRONTIER' TO THE 'LONE STAR STATE'

Within the United States, Southwest Foundation's Department of Genetics has several studies of large family groups in minority populations.

Under the direction and leadership of Dr. Jean MacCluer, a scientist in the Department of Genetics and leading researcher in genetic epidemiology, SFBR scientists are detecting and mapping major genes that influence susceptibility to heart disease, diabetes and obesity.

They also are characterizing the interactive effects of genes and environmental factors on these diseases.

## CARDIOVASCULAR DISEASE IN ALASKA, ARIZONA, OKLAHOMA AND THE DAKOTAS

With two major grants from the National Heart, Lung, and Blood Institute, the Department of Genetics is a national center for genetic epidemiological studies of Native American populations.

In a remote area of Alaska, the *Genetics of Coronary Artery Disease in Alaska Natives* project involves the study of the genetics of coronary artery disease in Eskimos. Twelve-hundred family members from native villages are part of this study.

Several Native American groups from Arizona, the Dakotas and Oklahoma participate in the *Strong Heart Family Study*. This project is characterizing the genetic components of susceptibility to heart disease in 3,600 family members of these groups. The study also involves a genomic search for genes influencing disease risk.

## HEART DISEASE, OBESITY AND DIABETES IN THE 'ALAMO CITY'

In Texas, the Department of Genetics is studying the genetics of heart disease in Mexican Americans. The *San Antonio Family Heart Study* involves 1,400 members in 40 extended Mexican American families living in San Antonio.

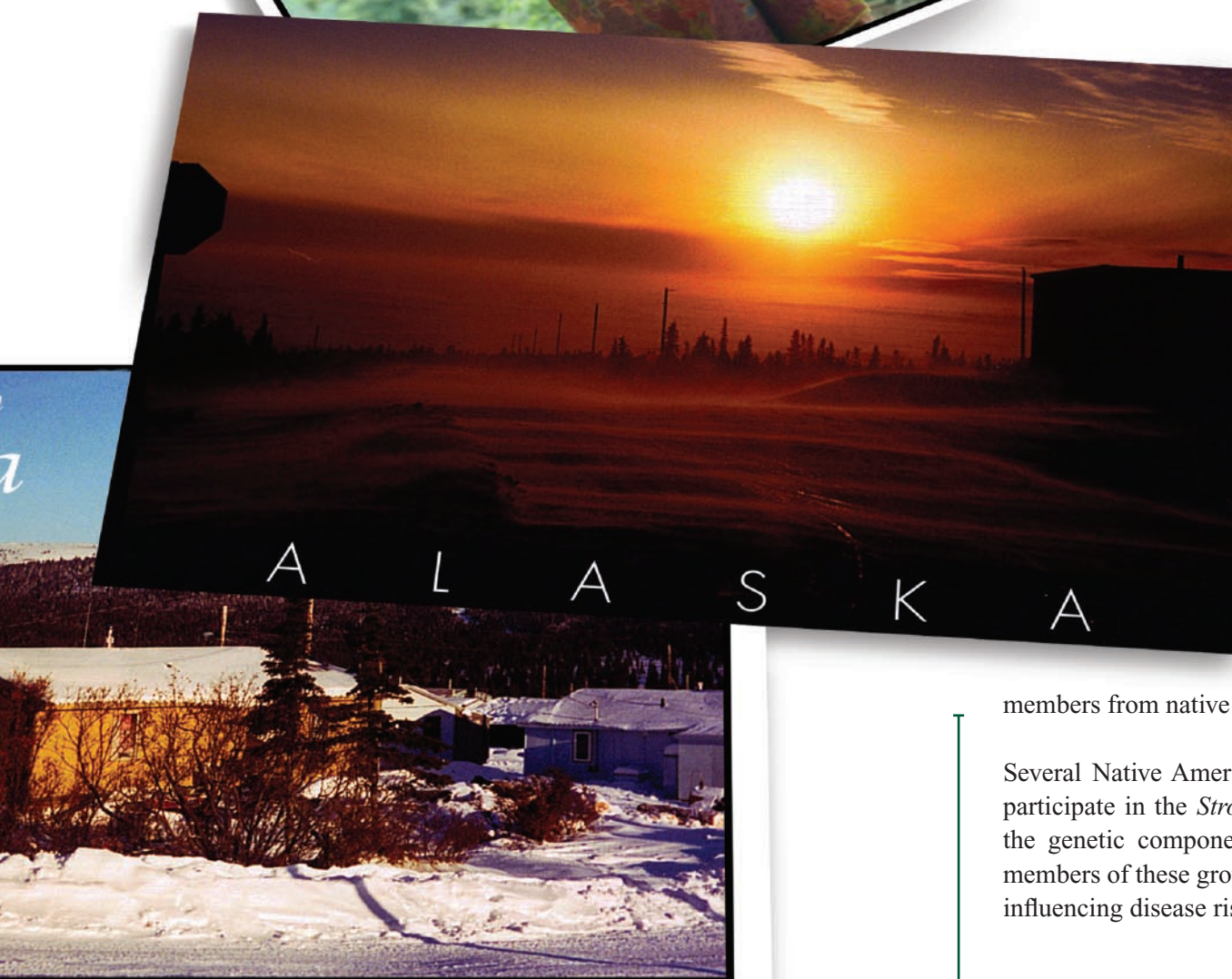
As part of this large-scale study, researchers also are investigating the genetic basis of two diseases so prevalent in Mexican Americans: obesity and non-insulin-dependent diabetes mellitus. These two common health problems greatly increase the risk of cardiovascular disease.

Under the study, Southwest Foundation scientists already have made several significant discoveries that show some individuals in the Mexican American population may be more susceptible to heart disease than others. To obtain evidence for disease susceptibility genes, researchers are analyzing patterns of variation in disease risk factors in the Mexican American families.

Already, Foundation geneticists have detected more than a dozen major genes that influence heart disease factors, found evidence for the influence of major genes on several obesity-related measures, and detected that insulin levels are influenced by a major gene, as is the age of onset of diabetes. Their long-term goal is to isolate these genes and to identify them.

Future research will determine how specific genes make some individuals more likely to have heart disease no matter what their eating or exercise habits are, and if maintaining a healthy lifestyle could prevent a specific gene from being expressed.

The *San Antonio Family Heart Study* involves a multidisciplinary team of scientific investigators in several laboratories at Southwest Foundation and at The University of Texas Health Science Center at San Antonio.



As an expansion of this infectious disease genetics program, Dr. Jeff Williams, an assistant scientist in the Department of Genetics, is developing the baboon as an animal model for Chagas' disease. Some of the Foundation's baboons are naturally infected with *T. cruzi* for life, making them an excellent animal model for understanding this important disease process. The methods and results from the baboon and human population studies will complement each other. The baboon study will increase knowledge about the basic biological processes underlying Chagas' disease. It will be of tremendous benefit in testing new vaccines and therapies as they become available.

Currently, there is no vaccine, effective treatment, or cure available for Chagas' disease. More than 16 million people are infected and another 100 million are at risk for infections with *T. cruzi*. This parasite is transmitted to humans from blood-sucking reduviid bugs that live in brush and in the Posse region's rudimentary houses constructed of mud-brick walls. *T. cruzi* has been found in the United States, raising national public health concerns.

## MALARIA PARASITES IN THAILAND

In Thailand, SFBR is conducting ongoing research on the genetics of drug resistance in the most lethal of the human malaria parasites, *Plasmodium falciparum*. This parasite, which is transmitted from one person to another by the female anopheline mosquito, has developed resistance to many antimalarial drugs. This resistance is hampering efforts to control malaria, which remains a global health problem that results in an estimated 2.7 million deaths per year.

Dr. Timothy Anderson, an assistant scientist in the Department of Genetics, has initiated an innovative research program focused on mapping genes for drug resistance in the parasites that cause malaria. The "*Mapping Drug Resistance Genes in Plasmodium Falciparum*" project uses blood samples drawn from individuals living in refugee camps along the Thai-Burmese border in Thailand.



With many health problems, your body tells you that something is amiss. But with high blood pressure, there are no symptoms. Stroke, heart attack, congestive heart failure or kidney failure can lurk just around the corner for those people who unknowingly suffer from uncontrolled high blood pressure. That is why hypertension is dubbed the “silent killer.”

Nearly a quarter of all adults in this country have high blood pressure, but one-third of these individuals don’t even know they have it. The cause of hypertension remains one of life’s mysteries. Drugs and heart-healthy lifestyle changes can help control hypertension, but much remains to be done to uncover this “killer.”

One culprit implicated in high blood pressure is salt. In its educational materials, the American Heart Association pushes the message: “*Shake your salt habit.*” Scientists believe that 20 to 25 percent of the human population is salt sensitive. These individuals should monitor their sodium intake as a preventive measure in keeping blood pressure under control.

The AHA recommends no more than 2,400 mgs of sodium per day, the equivalent of 1 1/4 teaspoons salt. Considering that sodium is both naturally and commercially added to food, sodium intake can really add up.

**SOUTHWEST FOUNDATION’S UNIQUE RESOURCE  
FOR STUDYING SALT-SENSITIVE HYPERTENSION**

Just what causes salt to play a bad role in blood pressure regulation for nearly a quarter of the world’s population? Do individuals inherit genes that make them susceptible to salt sensitivity and the blood-pressure problems it causes?

# Salt: An Accessory to the ‘Silent Killer?’

At Southwest Foundation, scientists are taking advantage of the research institution’s valuable pedigreed baboon colony to unravel the mysteries behind sodium-sensitive blood pressure.

With physiological, immunological, biochemical, pathological and genetic characteristics so similar to humans, the baboon makes an ideal animal model for disease-related studies. In particular, the baboon has proven to be an excellent model for studying cardiovascular disease and its associated risk factors, including hypertension.

Dr Robert Shade, scientific director and a scientist in the Department of Physiology and Medicine, has devoted his entire career to increasing our understanding of the disease processes that cause high blood pressure. Under the leadership of this internationally recognized physiologist, the Department of Physiology & Medicine studies the many factors contributing to blood pressure regulation in primates.

In collaboration with Dr. Joseph Haywood at The University of Texas Health Science Center at San Antonio, Dr. Shade recently received a 5-year, \$2.9 million grant from the National Institutes of Health (NIH) to study “*Angiotension, Sodium, and Genes in Primate Hypertension.*”

“This study should determine how important salt level is in the diet,” Dr. Shade says. “It will help answer the question of why salt sensitivity is a big factor in some individuals and not in others. This may lead to new methods of diagnosing people with salt-sensitive hypertension, and then ideally, to treatments for these individuals.”

Dr. Shade, in collaboration with Dr. Candace Kammerer in SFBR’s Department of Genetics, began a study of the genetics of hypertension 10 years ago. This study measured several biochemical markers associated with hypertension in human populations in the pedigreed baboon colony. One of these markers measured by Dr. Shade’s laboratory, red blood cell sodium-lithium countertransport (SLC), was found to be controlled by a major gene when Dr. Kammerer performed an initial genetic analysis of the data.

With the recent completion of a genetic linkage map of the baboon genome by Dr. Jeff Rogers, Dr. Michael Mahaney and their colleagues in the Department of Genetics, Drs. Shade and Kammerer were able to reanalyze the hypertension marker data collected from the pedigreed baboon colony. This analysis revealed that a major gene located on chromosome 5 was responsible for up to 59 percent of the observed variation in SLC.

Since high SLC is associated with inherited hypertension in human populations and, more specifically, salt-sensitive hypertension, Drs. Shade and Haywood will study the link between SLC





levels and sodium-sensitive blood pressure in the baboon. They will look for predictors of salt-sensitive blood pressure and study baboons with high SLC levels and those with low levels. This is one of the first studies addressing mechanisms of the relationship between salt, blood pressure regulation and salt appetite in the nonhuman primate.

“This research should answer questions about links between SLC levels and blood pressure,” Dr. Shade says. “It also may deepen our understanding of ‘metabolic syndrome’ as it relates to obesity and diabetes, two other major risk factors for cardiovascular disease.”

In the meantime, until the mysteries of salt-sensitive hypertension are unearthed, it’s best to cut back on sodium intake.

### TEAMING UP WITH THE UT HEALTH SCIENCE CENTER AT SAN ANTONIO

Each year, Southwest Foundation and The University of Texas Health Science Center at San Antonio collaborate on research projects in numerous areas of science. For the Health Science Center, Southwest Foundation’s unique resources, from its pedigreed baboon colony to its full-size neonatal intensive care unit to its maximum containment laboratory for studying lethal viruses, have proven to be of tremendous benefit to the Health Science Center.

Going beyond facilities, however, are the scientists at Southwest Foundation themselves. From serving as adjunct faculty at the Health Science Center to being co-investigators on millions of dollars in grants from the National Institutes of Health, SFBR scientists play an important role in the Health Science Center’s efforts to improve human health.

Dr. Robert Shade has been one of those SFBR scientists since his arrival at Southwest Foundation 19 years ago. In 1983, he began collaborating with Dr. Joseph Haywood, a professor in the Health Science Center’s School of Biomedical Sciences, on hypertension studies. That successful collaboration has been going on ever since.

“Our greater goal was to simulate cardiovascular research across species and to better understand human hypertension by using nonhuman primates,” Dr. Haywood says. “We can learn a lot from rats, but we need an animal model genetically and physiologically similar to humans for studying complex diseases that involve multiple physiological processes and multiple organ systems.”

Like humans, blood pressure regulation in baboons is highly dependent upon reflex mechanisms in the brain that control the activity level of the sympathetic nervous system. The sympathetic nervous system directly affects several organ systems involved in blood pressure regulation such as vascular smooth muscle, the heart, and the handling of salt and water by the kidneys. Scientists believe that diet and genetic factors can interact with the neural influences on kidney function to determine the level of long-term blood pressure regulation.

### A COLLEAGUE SHARES HIS THOUGHTS

Dr. Haywood is quick to point out the value of his collaborative efforts with Dr. Shade and Southwest Foundation.

“Bob Shade and I bring many years of experience and friendship to our work,” Dr. Haywood says. “There is a great synergy to our work. In our hypertension studies, I’m interested in how the brain transmits information and Dr. Shade in simulating the role of the kidneys. So the Foundation looks at hypertension from the bottom up, and UT from the top down. The mesh is perfect.

“I have many words to describe Bob Shade: commitment, integrity, intuitive, clear thinking. The list goes on,” Dr. Haywood says. “He is a great collaborator, one of the really innovative people in science in terms of his approach to science.”

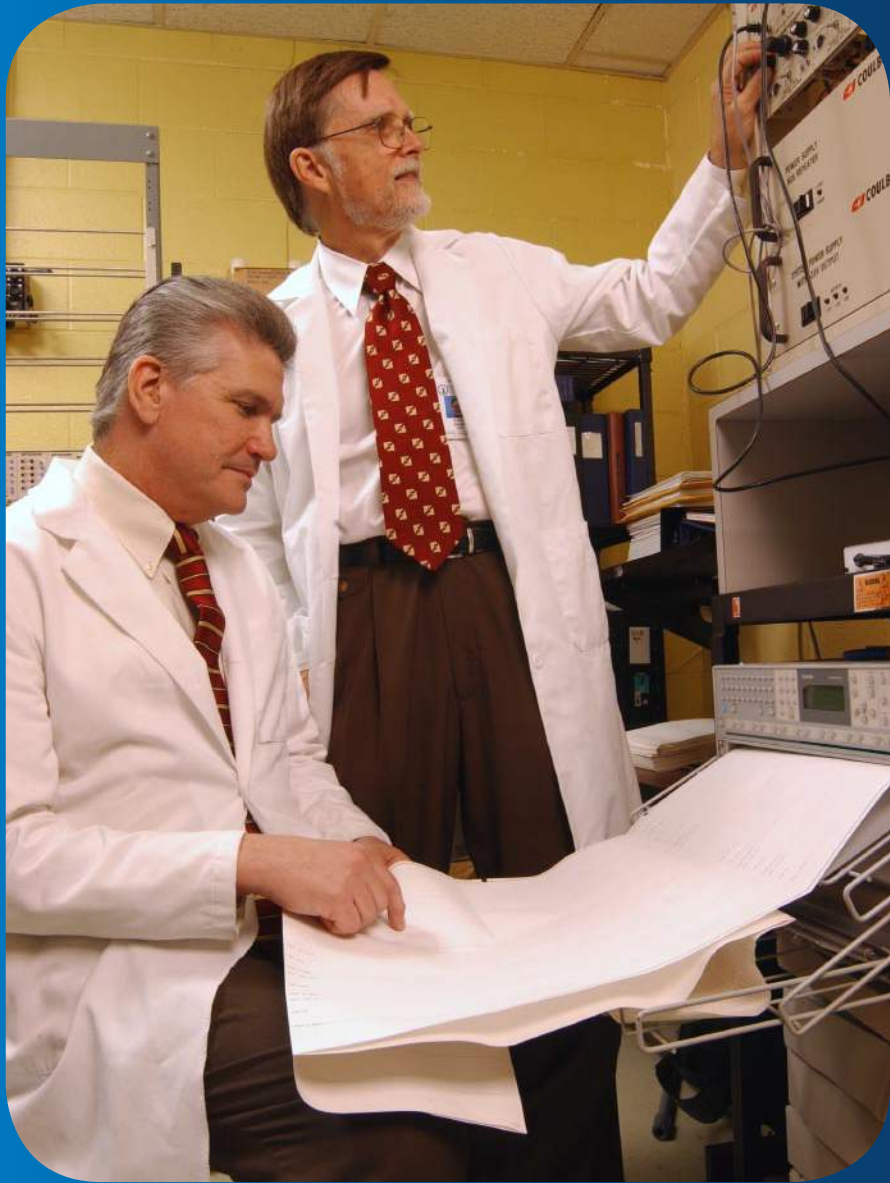
Dr. Haywood admires SFBR’s long and strong reputation of humane care of its animals, from its design of studies that use the fewest possible animals to get the greatest amount of data, to its highly dedicated veterinary staff.

“I think the whole city of San Antonio has been fortunate to have Southwest Foundation,” Dr. Haywood says. “This is such a unique facility. The potential is unbelievable here.”

### DID YOU KNOW?

- Blood pressure of less than 140 over 90 is considered a normal reading for adults.
- What do blood pressure numbers indicate?
  - The higher number represents the pressure while the heart is beating.
  - The lower number represents the pressure when the heart is resting between beats.
- The average American consumes about 6 to 18 grams or about one to three teaspoonfuls of salt daily. Your body actually only needs about a half gram of salt each day.
- Reducing the amount of sodium (salt) you consume may help you reduce or avoid high blood pressure. Adding fresh lemon juice to fish and vegetables is an ideal substitute for salt.
- Most foods in their natural state contain sodium. But most sodium in our diet is added to food while it’s being commercially processed or prepared at home.
- When buying prepared and prepackaged foods, read the labels. Many different sodium compounds are added to foods. Watch for the words “soda” and “sodium” and the symbol “Na” on labels — these words show that sodium compounds are present.
- Some over-the-counter drugs contain lots of sodium. A statement of sodium content must appear on labels of antacids containing 5 milligrams or more per dosage.

— From the American Heart Association







# Countering Bioterrorism

SFBR Plays a Key Role in UT's Promising Anthrax Antitoxin

*"If there is another outbreak of anthrax — whether naturally caused or as an act of bioterrorism — we will have more in our arsenal than antibiotics ... We look forward to taking this vital research to the next level in hopes of developing a possible cure for the deadly anthrax pathogen."*

— Dr. Jean L. Patterson  
Chairman

Department of Virology and Immunology  
Southwest Foundation for Biomedical Research

in the humane use of animals in research, new state-of-the-art virology and immunology laboratory complex, and esteemed scientists, the University knew it had the collaborator it needed to help the nation in its fight against biological warfare agents.

In April 2001 — months before the horrifying events of Sept. 11 — UT Austin researcher Jennifer Maynard contacted Dr. Jean Patterson, noted microbiologist and chairman of Southwest Foundation's Department of Virology and Immunology. Dr. Patterson was asked if her department would conduct animal experiments on a promising cure for anthrax that was based on powerful antibodies developed by biochemical engineers and chemists at the University.

UT Austin had been working on anthrax research for the U.S. Department of Defense (DoD) since 1997 through a long-term collaboration between Dr. George Georgiou, professor of biomedical and chemical engineering, and Dr. Brent Iverson, professor of chemistry. However, the University lacked the necessary protocols to conduct animal experiments with anthrax, which is considered a "select agent" by the Centers for Disease Control. Southwest Foundation, with its specialized laboratories, personnel and protocols, was a natural for the job.

Dr. Patterson accepted UT Austin's offer, and in an ironic twist of fate, conducted some of the animal experiments at the Southwest Foundation campus right in the midst of the country's nightmarish anthrax scare last October. Dr. Patterson, whose laboratory has done other research against biowarfare agents for the DoD, teamed up with Southwest Foundation veterinarian Dr. Kathleen Brasky for the animal experiments.

## ANTHRAX: BIOTERRORISM'S WEAPON OF CHOICE

Now a household word, anthrax (*Bacillus anthracis*) was one of the first biological warfare agents to be developed, and it continues to be a major threat. Anthrax is caused by a bacterium whose dormant airborne spores can enter the body by breathing or through a cut on the skin. Once inside the human system, the spores begin to actively reproduce. In the case of deadly inhalation anthrax, rapidly multiplying, toxin-laden bacteria soon make their way from the lungs to the bloodstream, and throughout the entire body.

When flu-like symptoms appear a week or so after the victim is exposed to anthrax, they're often disregarded at first. By the time the sufferer develops full-blown respiratory distress, it is usually too late. At that point, not only must the bacteria be killed, but its deadly toxins as well.

Anthrax microbes possess an arsenal of three toxins. The first, called protective antigen (PA), binds to the body's own immune cells. Working together in groups of seven, the PA molecules carry out a complex process that eventually punches a hole through the immune cell and "injects" the two other toxins, edema factor, which causes swelling, and the deadly lethal factor. The triple assault seriously disrupts the body's natural defenses and can lead to death.

## TESTING OF THE ANTHRAX-BATTLING ANTIBODIES

To counter the anthrax toxins, UT Austin focused its research on targeting that late stage, which is beyond treatment and fatal up to 80 percent of the time. The anthrax antidote was chemically engineered in Austin, and then tested in animals

at SFBR. For safety reasons, the researchers used laboratory-synthesized toxins provided by the National Institutes of Health (NIH) rather than real anthrax spores.







In Austin, Drs. Georgiou and Iverson genetically engineered a novel, “sticky” antibody that derails the anthrax PA toxin by providing an alternative, more attractive surface than with other available antibodies to which the destructive antigen can adhere. Once bonded to such substitutes, the PA toxin is rendered inert and harmless, alleviating the toxin-dependent symptoms of anthrax.

The protein antibody called “1H” bonded 50 times more tightly to the anthrax toxin than any antibody previously tested. It binds with the PA by offering it a more desirable docking surface than the blood cell.

“Having the antibody bind 50 times better means that it can hold onto the toxin long enough to have the entire complex cleared from the

body, eliminating the toxin before it has a chance to do any damage,” Dr. Iverson says.

“Combined with antibiotics, this could represent an effective treatment. The 1H antibody can be made quickly, inexpensively and in large quantities.”

On the Foundation campus, Drs. Patterson and Brasky administered the powerful new anthrax antibody to rats infected with the deadly pathogen. Their testing, which was finished last December, yielded an exciting result — the rats injected with the antibody survived a dose of anthrax toxin that was 10 times stronger than what would normally be a lethal dose.

These promising results went through extensive scientific review and were published in the June 1, 2002, issue of Nature Biotechnology. Joining Drs. Georgiou, Iverson, Patterson and Brasky as co-authors of the study, “*Recombinant Antibody Fragment Mediated Protection to Anthrax Toxin Challenge Correlates with Antigen Affinity*,” were Maynard, a UT Austin doctoral candidate at the time, and Dr. Stephen Leppla with the NIH.

“This finding represents an encouraging and significant step forward,” Dr. Patterson says. “This has been a very effective collaboration with UT, a perfect fit. Our goal is two-fold. We are trying to block replication and the effect of the toxin.”

## NEXT STEPS TOWARD A CURE

Further trials are necessary to determine the antibody’s effectiveness in humans and the best treatment methods. The antibodies theoretically would be administered by injection to persons exposed to anthrax and would block the toxin’s deadly effects. This new antibody treatment, coupled with a concurrent regimen of antibiotics, would disable both the anthrax toxin and its related bacteria.

The next phase of research, also to be performed at Southwest Foundation in conjunction with EluSys Therapeutics Inc., will involve reformulating the antibody to last longer in the body.

Later studies will involve testing the antibodies against the anthrax bacteria itself, rather than just the toxin produced by the bacteria. This testing will be done in SFBR’s biosafety level 4 (BSL4) laboratory, one of the world’s premier research facilities for studying emerging and deadly infectious diseases in complete safety for the scientists and the environment. In this maximum containment laboratory — the only privately owned BSL4 in the country — scientists wear space suits to study deadly bacteria such as anthrax.

Although human trials with the antibodies remain several years away, the results of the UT Austin and Southwest Foundation collaboration are encouraging. So far, it appears to be the most advanced research done on anthrax toxins.

“If there is another outbreak of anthrax — whether naturally caused or as an act of bioterrorism — we will have more in our arsenal than antibiotics such as Cipro, which are not effective if taken too late after infection,” Dr. Patterson says. “We look forward to taking this vital research to the next level in hopes of developing a possible cure for the deadly anthrax pathogen.”





# 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. Southwest Foundation must rely on private philanthropic investment.

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

## Southwest Foundation Forum

With unbridled enthusiasm and hard work, the women of the Southwest Foundation Forum serve as dedicated supporters of Southwest Foundation. The Forum promotes SFBR's research programs through community relations, volunteer service efforts and fund-raising activities.

The exceptional women who have led the Forum throughout its history were honored at a past presidents' luncheon at The Argyle March 25. The group assembled on the steps of The Argyle for the photo above. Pictured below with SFBR Chairman John Kerr are, *left to right*, Ruth Eilene Sullivan, Tena Gorman and Dottie Block, the trio who organized its founding board in 1970. Ms. Block is holding a poster promoting the Forum's first gala.

The group's glamorous, fun-filled gala has become one of San Antonio's premier social events, raising nearly \$2 million to support basic biomedical research at SFBR. Under the presidency of Maureen Mimari, the Forum's "East India Trading Company" gala was May 2 at La Villita Assembly Hall.

**For information about  
joining the Forum, please contact  
Ms. Francie Calgaard at (210) 822-7315.**



It was a wonderful and successful 2001-2002 Forum year! Highlights include our Science Education Awards to area high schools, the student tours of Southwest Foundation, and our fabulous gala.

Five high schools had the honor of receiving the coveted grants from the Forum and the V.H. McNutt Memorial Foundation. Winning high schools include: Roosevelt, first place; Jourdanton, second place; Memorial, third place; Keystone, fourth place; and Harlandale, honorable mention. As a special bonus established a few years ago, all schools submitting a grant proposal received a participatory award from the L.D. Ormsby Foundation. We also are indebted to the Southwest Foundation scientists who every year serve as judges for this event.

Once again, the student tours were a hit with area high schools. Nine area high schools had the privilege of touring the Foundation campus and meeting some of its outstanding scientists. Many Forum members served as docents for the tours — this remains a great volunteer opportunity for our Forum membership. This is such a unique program and so special for high school science classes.

We ended our year with the most fabulous gala in our history! "East India Trading Company" was executed so beautifully with the decorations, food and favors all reflecting the exotic theme. Villita Assembly Hall has never looked so beautiful! The games were so creative and the prizes the best ever! It was a great idea to have a special category for those 35 and younger so that they too can begin to support Southwest Foundation.

It was an honor to serve as president of the Forum, and a highlight among my volunteer activities! We made great strides and added to the legacy established 32 years ago by our founders. I appreciate the special gifts and talents that each board member so readily shared to promote our mission "to serve the Southwest Foundation for Biomedical Research through community relations, volunteer service and fundraising."

Maureen Mimari  
2001-2002 President  
Southwest Foundation Forum







# The East India Trade Company The Gala 2002



## The Founder's Council

Community leaders between the ages of 25 and 46 belong to Southwest Foundation's Founder's Council, which was formed to honor Tom Slick, Jr., who was only 25 when he founded SFBR, and just 46 when he died in 1962. Richard M. Peacock, Jr. currently serves as president of The Founder's Council.



The Founder's Council assists Southwest Foundation by supporting and raising awareness of SFBR's critical mission to conduct research that improves health and saves lives. Each member's minimum annual contribution of \$100 helps fund specific research projects at Southwest Foundation and also allows The Founder's Council to sponsor a series of luncheons and other events throughout the year.

The photographs to the left were taken at the group's spring 2002 events at The Argyle. At the March 7 luncheon, SFBR's Dr. Tim Anderson's presentation, *"Parasites Fight Back ... Drug Resistance in Malaria,"* gave members an inside look at the most lethal of the human malaria parasites, which has developed resistance to antimalarial drugs. Malaria causes more than 2 million deaths each year. At the May 30 cocktail reception, SFBR's Dr. Anthony Comuzzie's presentation, *"Do Your Genes Determine the Size of Your Jeans,"* featured his work on the relationship between genes and susceptibility to obesity, which is a major risk factor for diabetes and heart disease.

In the fall, The Founder's Council has a Sept. 25 luncheon and presentation at The Argyle, an Oct. 11 evening tour with Forum members at the Southwest Foundation campus, and a Dec. 11 Christmas party.

*For membership information on The Founder's Council, please contact Mr. Richard Shemwell, (210) 829-7003.*

## The Golden Circle

Since 1977, members of The Golden Circle — individuals, corporations and foundations who firmly believe in the continuing value of basic biomedical research — have contributed more than \$27 million to Southwest Foundation's research programs.

Members of The Golden Circle contribute \$1,000 annually to Southwest Foundation. The Corporate Circle is the business equivalent of The Golden Circle, with membership based on a minimum gift of \$2,500 per year. Membership in The President's Circle, which augments the philanthropic level of The Golden Circle, is based on an unrestricted donation of \$5,000 or more per year.

In November 2001, Golden Circle members were honored with a Southwest Foundation cocktail buffet at the home of Mr. and Mrs. Hugh Halff, who are pictured to the left with Dr. and Mrs. Ricardo Romo. The photos below also were taken during the fall reception at the Halffs.



*To inquire about membership in The Golden Circle, contact Mr. Albert Steves IV, director of special projects, Southwest Foundation, (210) 258-9409.*







**John Blangero, Ph.D., a scientist in SFBR's Department of Genetics, is the first Foundation researcher to be selected for a MERIT Award from the National Institutes of Health.**

***This prestigious honor is bestowed on less than one percent of NIH-funded researchers during their scientific careers. Dr. Blangero is widely recognized as one of the world's leading statistical geneticists and as a pioneer in the methods for identifying genes influencing common complex diseases.***

*Your winning the MERIT Award from the National Institutes of Health (NIH) certainly testifies to the tremendous impact of your scientific endeavors in genetic research. What are your endeavors outside of the laboratory?*

Travel ... my job entails a lot of travel all over the world. I traveled 170,000 miles last year. What a life for such a simple guy. But my real outside gig is singing.

In every city my work takes me to, I try to find some place to sing, whether it's Barcelona, Spain; Melbourne, Australia; or Paris, France. You could call me a "karaoke hustler." I bring in my own discs, especially in foreign countries.

Doing karaoke in Paris, wow! I dropped in a place just off the street. It was a high-end karaoke venue with seasoned pros and fantastic sound, a big deal with serious singers. I was just the outsider, and an American to boot. I sang my rendition of "Brandy, You're a Fine Girl," and wowed the crowd.

*In your work, you develop advanced statistical genomic tools to discover the specific genes that influence common complex diseases. What "tools" do you use outside of work?*

At home, I have a full karaoke set-up because if you are serious about it, you have to practice. Although you pretend like it's your first time up there on stage, in fact, you are trying to win the crowd over.

I always carry around some kind of music system because I'm always listening to music. I'm an old rock 'n' roll guy. I used to be in a band back in the '70s, and I still pretty much only listen to music that was developed from 1968 to 1980.

And I always carry about 20 karaoke discs with me that have MY favorite songs on them. Again, those are usually songs from about 1968 to 1975 or

## **John Blangero, Ph.D.** **Scientist, Department of Genetics** ***"Rock Star"***

so, because now as I'm getting older, all the karaoke places have a lot of the more recent stuff. The old guy likes to sing rock 'n' roll.

*What is your favorite number to sing?*

It varies a bit, but right now I'm really stuck on an old Ides of March song called "Vehicle." And at the end of the night, if the place is really jumping, I'll finish with "Born to Run," which is considered the karaoke "Holy Grail." It's one of those songs few people ever dare to try.

*Hmmm, the "Bruce Springsteen" of karaoke?*

I use the same name for karaoke. I always call myself "Dr. John." If you look up the Melbourne karaoke scene, Dr. John will be well known.

*When was the fork in the road when you decided to forsake your "rock 'n' roll" roots and go into science?*

That happened in 1979. My band worked from about 1970 to 1979. The name we were best known under in the area around Pittsburgh and Cleveland — I'm from New Castle, Pa., about 40 miles east of Pittsburgh — was "Harlequin." We were back in the "glam" days, and we used to wear a lot of tights and makeup and all that stuff. We had huge amounts of equipment and played our music at outrageous decibels.

When I had to choose to go to graduate school, I knew I wasn't going to be able to keep singing. We'd really gone as far as we were going to go. We'd been shopping our demos around to all the record labels without a lot of interest, and I thought I could make it in science. I knew — or so I thought — that science was going to be a lot easier than rock 'n' roll, so I took the "easy" path. Now I wish I had gone into rock 'n' roll, I think. *(Laughter)*

*You joined Southwest Foundation in 1986 as a postdoctoral research scientist. Describe yourself then, and then now, 16 years later.*

When I came to the Foundation in 1986, I tried to become more conservative at that period. My hair was short, and I wasn't doing any singing. I was taking getting into science very seriously.

But what I was called on to do at the Foundation was something that required a lot of imagination. Essentially I had to come up with solutions to problems previously thought to be intractable. So I basically had to do a lot of thinking and a lot of math.

But as we started to be successful and I started to give talks, I realized that I really liked being up in front of crowds. Being conservative was not natural to me at all.

I'm a pretty flamboyant guy, a flamboyant speaker. So I decided to start treating my talks more like rock 'n' roll events, trying to have more stage

# the **i** in science



presence. The next thing I knew, I was getting a lot of requests for speaking. So I've always thought that science was a lot like rock 'n' roll. I was starting to develop entourages at meetings, and I enjoyed that.

Once I got my scientific legs and figured out where I was going, I came around more to my true personality. I let my hair grow long again, and I started to wear long 19<sup>th</sup> century French frock coats when I would give a talk. Now, I just try to be a little off the beaten path in terms of how people think of most scientists.

I think it follows from my creativity to certainly not be bound by convention. When you are trying to come up with solutions to problems, you take the road less traveled.

*So you find that your extroverted personality has helped you in the science field itself?*

Yes, it has. Being a little bit more extroverted certainly helps when you are involved in public speaking. Public speaking is a major way to create an impression and to get people to listen to what your science is all about. Probably the best thing for my career — besides the fact we have done a lot of really good science here — is the fact I learned early on how to be a good public speaker. I get a lot of requests from all over the world now.

*Your research program's computer software package, SOLAR, is used by scientists worldwide, which requires you to travel to the far ends of the globe. What has been your most adventurous trip?*

It's got to be our work in Nepal, because it's so far off the beaten track. We've been going there a long time, and have seen a lot of changes in that country. Nepal is definitely an exotic site. I prefer five-star hotels, and there, well, I get the equivalent of a negative five-star hotel that barely has running water. And especially now, given the problems that Nepal has socially and politically, it's a rather adventurous place to visit.

When we worked in Tibet for a while, that was another adventure. Tibet was an exotic and incredibly beautiful place, at 4,000 meters high on the Tibetan Plateau.

Probably my favorite place to go of all is Barcelona, which I consider to be the most beautiful city in Europe. We have a good collaboration there on thrombosis that requires me to go there several times a year. Barcelona's a great place because it has fantastic food and incredible live jazz venues. People who have spent much time in Barcelona fall in love with the city.

*You work closely with other scientists in Southwest Foundation's Population Genetics Laboratory in developing powerful new methods for gene localization. What would your colleagues be most surprised to learn about you?*

They probably know everything about me. I doubt there's anything they really don't know. They pretty much know about my personality and what I like to do. Well ... some of them don't know that I'm really interested in modern art and like to go to the museums.

*You are the first Southwest Foundation researcher to be selected for a MERIT Award from the NIH. What does winning this "Grammy" in science mean to you?*

That was really gratifying because it's based on what your peers think about you. Having reviewed grants, it's really a satisfying thing to know that a large group of your peers thought your grant was so superior. You had to

not only pass through peer review, but programmatic review as well, so that means that the NIMH (National Institute of Mental Health) also thought a lot about your scientific program.

When our grant was reviewed, it scored in the .3 percentile, which is as low as you can get, and that means it's great. We knew we had hit a home run. And then when they gave the MERIT Award on top of that, it's research for as long a period as you can get. I'm just glad I won't have another major grant application here in five years for our theory program. So yes, it's a scientific "Grammy."

*What would you like to see most during your scientific career?*

Just to go the rest of the way. We've located genes, we've identified genes, and we've found the mutational variations in genes that lead to risk for some diseases. But what would be really nice would be to have one of these things — these results — translate into some true benefit to the public health. For example, the identification of a novel gene that leads to a new drug target. And we actually have some potential in that area.

So, it would be to take it further. Really I'm more interested in scale now, and that's just to have us be among the biggest and the best, and to have everybody all over the world point to Southwest Foundation as having been pioneers in the new era of human genomic solutions to common diseases.



***"Dr. Blangero's work is at the cutting edge of human genomics research. His methods are premier research tools for identifying genes that produce vulnerability to complex human diseases. Therefore, his scientific contributions are expected to have a profound effect on improving the public health."***

— Dr. Steven Moldin  
Chief, Genetics Research Branch  
National Institute of Mental Health



# Red McCombs

Continued from page 3

I think one area where we could make some impact is to acquaint more of our students with the Foundation. We have a great student population in the many colleges and universities in this area and of course, a large high-school population. It would take some programs we don't have in place during their formative years to impress upon them the importance of science. This is a great opportunity.

*What calls would you make for the city of San Antonio?*

I would call for the political leadership of the city to have a better understanding of the investment that could come from accelerating the growth of the biomedical industry in San Antonio. This would create jobs and opportunities in the workplace, as well as opportunities for a better quality of life. I think we can do a lot better in that area. San Antonio has many needs. Some are more obvious than others.

*You have a big game tomorrow. How do you prepare?*

My role is to try to give the players who are playing the game as many of the tools as I can to prepare them, and then to be a positive factor in that preparation. I always believe you can win every game.

*Are you an offensive or defensive player?*

I'm an offensive player, whether in sports or anything else. Offense is fun. There may be some disagreement with that, but I want to be the guy that scores the most. I'd just as soon be on the scoring side. I do get a pleasure out of it. I'd much rather score more than him.

*In life, do you enjoy nail-biting battles that go down to the last tick of the clock or do you prefer the big blowout? What makes you get pumped up about life?*

I like to get ahead and stay ahead. I've experienced plenty of nail biters, plenty of losses. I don't make any bones about that. My feelings are always on my sleeves. Sports are a defining element that defines wins and losses in a quick time frame.

*What have been some of the most meaningful victories in your life?*

I think any victories have always been day-to-day exciting elements of a day-to-day experience. I'm very much a "today" type of person. I don't look at my 74-plus years as being filled with certain momentous situations. I look at it as daily experiences. Daily opportunity is what I find very exciting.

*If Sports Illustrated were doing its preseason rankings, how would Red McCombs fare? As a man of great accomplishment, how do you remain so strong season after season?*

All the people show very little respect for this upcoming season. I'm sorry they missed the story because we are going to do very well.

Season after season? I consider it a pure joy to embrace the opportunities that each day brings. As problems arise, I turn them into opportunities. I don't always succeed, but there's always an exciting element to

look forward to. Also, I am a strong believer that every single day, I could get better at whatever it is that I am doing, and I try to do that.

In that, I don't equate it to business, I equate it to life. Whether you are a parent, a friend, or an associate, I think that is an option all of us have every day.

What do I do when I lose? First, I get angry. I try to temper it as quickly as I can, then I get sad, then I start thinking about tomorrow, and then I get excited.

I realized during my first year with the Vikings, with our longevity of wins and no losses, that my younger grandchildren had never experienced a loss. When the Vikings lost the conference final in overtime to Atlanta, one of the things that moved me was that I needed my wife, Charline, to explain to the younger grandkids why losses occur.

I've never been prepared for a loss. I think, as we look at the Foundation today, that we have reason to believe that every day is another step toward wins.

*Will San Antonio ever land an NFL team?*

It's difficult to get an NFL team because the structure of the league is such that there are 32 teams, and 32 teams only. It would be necessary for an existing team to leave its current city and move to San Antonio.

I think San Antonio deserves a team, and would very well support a team. A major-league sports franchise is a great asset to any city, adding to that community's opportunities. I think that sports play a great role in the psyche of the community, and to that end, I think a sports team is just as important to the people who don't attend games.

When the Spurs moved to San Antonio in 1972, they had no following. We had to build a fan base for basketball in the city. When the Spurs captured the NBA championship a few seasons ago, however, that championship permeated every element of the city in a positive way.

