

PROGRESS

A Publication of the Southwest Foundation for Biomedical Research

Hope in the Himalayas:

Nepal study improving lives today and tomorrow

Page 3

INSIDE:

Clearing hurdles in race to defeat a 'silent epidemic'

Page 7

Cancer's newest enemy: Tiny opossum has big impact

Page 10, 12

The "I" in science: Dr. Hayhurst an engineer for better health

Page 14

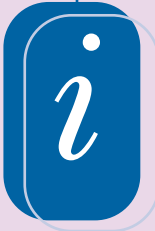
In the spotlight: Trustee Louis Stumberg

Page 17



President's Column

Dr. Frank F. Ledford, Jr.
President



nnovation. Future advances in health care depend on it, and I believe it can be found in plentiful supply at the Southwest Foundation for Biomedical Research. Our scientists share a commitment to the exploration of new methods for combating disease, a commitment that shines forth in this issue of *Progress*.

In April, two of our scientists – Dr. Robert Lanford and Dr. John Blangero – were honored by the *San Antonio Business Journal* as health care heroes. A previous issue of *Progress* highlighted the accomplishments and interests of Dr. Blangero, a world leader in the field of statistical genetics. Now, on pages 7-8 of this publication, our readers can see why Dr. Lanford is so deserving of this award. Among his other accomplishments, he recently published the first evidence that a vaccine is possible against all strains of a silent killer, hepatitis C. This work was done with chimpanzees, the only animal besides man susceptible to hepatitis infections, demonstrating why nonhuman primates are so important to biomedical research.

However, you might be surprised to learn how studies with the lowly worm and opossum also can be of immense value to humanity. An SFBR study in Nepal on worm parasitism has the potential to improve the lives of millions who suffer from worm infections as well as a broad range of other ailments.

Meanwhile, a small South American opossum has provided our scientists with a revolutionary model of human cancers and given them a vision of ways to offer individually tailored cancer treatments. Among its other unique potentials, the laboratory opossum might also provide us with insights on spinal cord repair. This topic is particularly dear to my heart, since as an orthopedic surgeon, I have seen how helpless we currently are in efforts to treat these devastating injuries.

“Innovator” is certainly an appropriate description of one of SFBR’s newest scientists, Dr. Andrew Hayhurst. Don’t miss “The ‘I’ in Science” if you want to see how this bright young man is exploring treatments and vaccines for anthrax, SARS, and various emerging infectious diseases.

And through our trustee spotlight, you will be introduced to one of my personal heroes, Louis Stumberg. I knew and admired Mr. Stumberg as a great patriot long before I came to SFBR. As the longest-serving civilian aide to the secretary of the Army, he has served his country through many presidencies, political regimes and international conflicts. A great American, he also shares SFBR’s passion for the exploration of new frontiers.

As you thumb through these pages of *Progress*, I hope that you, like me, will be inspired by those who quietly work to bring about advances that today exist only in our dreams.

Fine French suits a perfect fit for ‘hot zone’

Thanks to a generous gift from the Edouard Foundation, researchers are donning new, custom-made French suits when they work inside SFBR’s maximum containment laboratory. The suits are not made of fine silk or wool, but rather, of fabric-backed PVC that helps protect them from the deadly pathogens they study inside the biosafety level four (BSL-4) laboratory, things like Ebola, Lassa fever, Crimean Congo hemorrhagic fever, and SARS.



Dr. Jean Patterson, chair of Virology and Immunology at SFBR, shows Ron and Valerie Finch the beneficial features of the new “spacesuits” that the Edouard Foundation recently donated to the BSL-4 lab.

The New York-based Edouard Foundation recently donated a dozen of the \$2,000 suits to help make the scientists’ challenging BSL-4 work a little easier.

Offering the first redesign of a BSL-4 “spacesuit” since the 1950s, these suits by French-based Delta Protection provide equal safety with added comfort. They are lighter weight and sit better on the shoulders than the older suits, enhancing scientists’ mobility and decreasing work fatigue. The clear headpiece also allows an unrestricted field of vision.

Researchers were delighted when the new suits arrived in March. When Dr. Ricardo Carrión, Jr. tried his on for the first time, he remarked, “I love how comfortable this is. Sometimes we spend three to five hours in the BSL-4, and in the old suits, our shoulders would ache and our arms would get so tired. That’s not going to be a problem anymore.”

Ron Finch, a board member for the Edouard Foundation, along with his wife, Valerie, came to SFBR on April 2 to see the new suits. “We’re happy to provide something that better enables life-saving research,” Mr. Finch said. “SFBR’s scientists have access to extraordinary facilities here with the BSL-4, but the previous suits put stricter limits on the amount of time they could physically devote to their laboratory research. The chance to offer something that could lift those limits was very appealing to us.”

He added that, since family members of the Edouard Foundation have historical ties to France and some of its board members live in San Antonio, “It’s nice to see the French contribute to outstanding science that is taking place right in our own backyard.”

PROGRESS

Editor and writer: Julie Collins, director of communications

Design and production: Jeffrey Heinke Design

Photography: Clem Spalding, Joan Snow, Geno Loro and Sarah Williams-Blangero

Progress is a publication of the Southwest Foundation for Biomedical Research. If you would like to be added to our mailing list or to update your mailing information, contact Julie Collins at (210) 258-9437.

A photograph of a woman in a red headscarf and green sweater holding a child in a white hat. The woman has a nose ring and is smiling slightly. The child is looking towards the camera with their hand near their mouth. The background is a blurred outdoor setting.

Hope in the Himalayas:

Nepal study has broad applications, humanitarian benefits



Children suffering from worm infections that stunt their growth and cognitive development ... An elderly woman whose bones are weakening from osteoporosis ... A young adult recently diagnosed with schizophrenia ... The increasing number of people in the United States affected by obesity ... Impoverished families in the Himalayan foothills who lack access to basic health care ...

Continued on page 4



The Jiri Helminth Project is improving the lives of the Jirel population today as it offers hope to people around the world for a healthier tomorrow.

Hope, continued from page 3

What do all these people have in common? They are beneficiaries or potential beneficiaries of the Jiri Helminth Project, a research program initiated and led by Dr. Sarah Williams-Blangero, chair of the Genetics Department at the Southwest Foundation for Biomedical Research.

The project works with a large family group in southern Asia in the region of Jiri, Nepal, trying to learn why some individuals are highly susceptible to worm infections while other people living in a similar environment show resistance to infection.

Dr. Williams-Blangero and her colleagues have made some key discoveries in this area of research in recent years. They also have seen their original study branch off in a number of interesting directions as scientists at SFBR and other institutions have developed new studies relying on the same family group. The most recent example is a new grant awarded by the National Institutes of Health (NIH) to Harvard University, in conjunction with SFBR, to study the Jirel population for genetic contributors to psychiatric diseases.

In the process of all this research, the Jirels – as well as individuals from numerous surrounding villages – benefit from the only source of health care for miles around,

made possible by the Jiri Helminth Project and related donations.

Program history and purpose

The project got its start in 1993, when Dr. Williams-Blangero and her husband, Dr. John Blangero, initiated a pilot study in Jiri to investigate genetic contributions to helminthic infections, or infections by parasitic worms such as roundworm, whipworm and hookworm. The program expanded greatly after an NIH grant award in 1995.

The Blangeros had worked with the Jirel population in the 1980s on an unrelated genetics project, so they already had good rapport with the government and the people. They also understood the plight of the Jirels and how this unique, isolated family group could provide valuable assistance to genetic researchers.

“In all areas where helminthic infections are common, 10 percent of the human population harbors 90 percent of parasitic worm infections,” said Dr. Williams-Blangero. “The question has always been, ‘What makes that 10 percent different?’ For years, everyone believed the difference was due to environmental factors. Environment does indeed play an important role, since these infections are transmitted through contaminated soil, but our experience with the Jirels



Even the youngest study participants get the opportunity to sign the consent forms their parents have approved.

told us there also are genetic factors at play.”

She explained that in Jiri, where the people all live in a similar environment, 65 percent of the population suffers from some type of worm infection, while 35 percent have no infection at all. Within the infected group, the degree of infection varies drastically. One individual might harbor only a few worms, whereas his neighbor might be infected with 250. “So genetic influences are evident,” Dr. Williams-Blangero said.

She knew that if she wanted to uncover those genetic influences, Jiri was the perfect place to start searching.

“The Jirels can be described as a hybrid population in that they trace their ancestry over nine generations back to two ethnic groups from their region of Nepal,” explained Dr. Williams-Blangero, “and they have remained biologically isolated, only marrying within their group. There are approximately 4,000 individuals in this group, all living within nine nearby villages and all engaged in similar lifestyles in similar environments. They are subsistence farmers who eat similar diets, earn the same level of income, and live in similar housing conditions. All these factors work together to create a unique and powerful human pedigree that is ideally suited for the study of genetic contributors to disease.”

The group of subjects volunteering for the study includes 2,000 family members, with information gathered on a total of 8,000 living and deceased relatives, making this currently the single largest human pedigree for genetic analysis. Such an extensive human pedigree has served as an invaluable research tool, leading researchers to some groundbreaking accomplishments.

Major accomplishments

In 1999, Dr. Williams-Blangero and her team published the first strong evidence that susceptibility to worm infections is heritable. That discovery was followed in 2002 with another publication in which the group showed the first explicit evidence of a specific, individual gene influencing susceptibility to helminthic infection.

The gene localization was based on a highly informative branch of the Jirel pedigree containing about 500 members. However, future analyses will be able to consider information from all members of the pedigree simultaneously as a result of SFBR’s greatly expanded analytical computing power now available through its SBC Genomics Computing Center. Since the center opened in June 2003, allowing SFBR to more than triple the size of its parallel processing network dubbed the “computer ranch,” SFBR scientists have had the ability to perform analyses on the more powerful extended Jirel pedigree. Already, they have localized four additional genes influencing

susceptibility to intestinal worm infections.

These findings are important to future methods of prevention and treatment of helminthic infections, which affect 25 percent of the world’s population. As Dr. Williams-Blangero explained, “The identification of mechanisms of natural resistance to a specific disease can aid in the development of drugs and other interventions that mimic natural human defenses against the disease.”

But the scope of Dr. Williams-Blangero’s work goes beyond worm infections. “While we’re focusing on these parasitic diseases as important disease entities themselves, we also are looking at them as model infectious organisms for the development of genetic research applicable to all infectious diseases,” she said.

Spurring new areas of research

In addition, the original work she and her colleagues did in establishing the Jirel pedigree is now making it possible to study genetic influences on a wide variety of health conditions, some related to parasitic infections and others of a far different nature. “Once you have established the pedigree and collected genetic data and samples from this extended family, that same data can be used in new studies of other health- and disease-related traits,” said Dr. Williams-Blangero.

Growth and development. For Dr. Brad Towne at Wright State University, that means looking at issues related to growth and development in the Jirel population. Because high worm loads exert a burden on children’s growth and cognitive development, Dr. Towne, with a 2002 NIH grant award, is studying the group to examine genetic influences on growth and development in an environment that includes parasitic worms.

Obesity. SFBR’s Dr. Harald Göring is working with the Jirels to study obesity in a lean population. The Foundation’s San Antonio Family Heart Study, led by Dr. Jean MacCluer,

Continued on page 6



The Jiri Helminth Project staff includes U.S. investigators, physicians from Nepal's leading school of medicine, and local nursing staff and research assistants.

Hope, continued from page 5

has identified a number of genes that influence obesity in a population that tends to have high rates of obesity. Now Dr. Göring is asking, "What are the effects of these genes on similar traits in a lean population? Do these genes only become evident in response to a high-fat, high-cholesterol diet that leads to obesity, or are the genetic components of these traits the same in a population that is very lean and has a high level of exercise?" In other words, are the same genes there but not activated in a lean population? A recent grant award from the San Antonio Area Foundation is helping him investigate this question.

Osteoporosis. Dr. Michael Mahaney, also a scientist in SFBR's Department of Genetics, is working with the Jirel population to study bone density and genetic issues related to osteoporosis.

Psychiatric disease. As mentioned above, Harvard University recently received an NIH grant to study the genetics of psychiatric endophenotypes – or traits that are predictive of psychiatric disease – in the Jirel population.

"Working with us, Harvard can study the genetics of psychiatric disease using the Jirel pedigree even though there is not a high level of psychiatric disease in that population," said Dr. Williams-Blangero. "All people have traits – with a normal range of variation – that are related to psychiatric disease, and researchers can study which genes influence even that normal variation. The situation is similar to cholesterol and heart disease. Everyone has blood cholesterol, even if they don't have heart disease, and researchers study which genes influence cholesterol levels both in patients who have heart disease and patients who do not."

Saving lives now

It is hoped that the ever-increasing scope of research in Jiri will lead to a variety of new prevention and treatment methods for a broad range of diseases. Today, however, the study is having an immediate positive impact on the Jirel people.

To conduct their research, scientists need to clear the people of their worm infections. For this reason, the project employs a medical team to operate a local clinic where they can see patients and administer antibiotics. This alone has been beneficial to patients with high worm loads, which in addition to stunting growth in children can cause anemia, rectal prolapse, and potentially fatal intestinal blockages.

But as one can imagine, study participants often are diagnosed with other health problems besides their helminthic infection, and even people who are not part of the study travel from surrounding villages seeking medical treatment. The doctors and nurses at the clinic volunteer countless hours of personal time for these extra services, and donations from people in Nepal and the United States pay for many of the patients' medications. In more than one case, an ambulance donated to the clinic by a church group has been used to transport patients on a 12-hour ride to Kathmandu for necessary specialty care.

"Although the medical care we provide is minimal by American standards, it is estimated that over 200 lives have been saved during the last two years of this research project," said Dr. Williams-Blangero, "and many times that number have enjoyed improved quality of life through the availability of simple medical services."

In this way, SFBR scientists are helping to save lives today and for generations to come.

Attacking the silent killer:

New evidence gives hope for successful vaccine against hepatitis C



It's the leading cause of liver failure and liver transplantation in the United States, described by some as the greatest health threat of the 21st century, but many people who have hepatitis C don't even know it until it's too late.

Hepatitis C has rightfully earned the name "silent killer" because of its tendency to quietly attack a person's liver for 20 or 30 years without causing noticeable symptoms – that is, until it has led to cirrhosis or liver cancer.

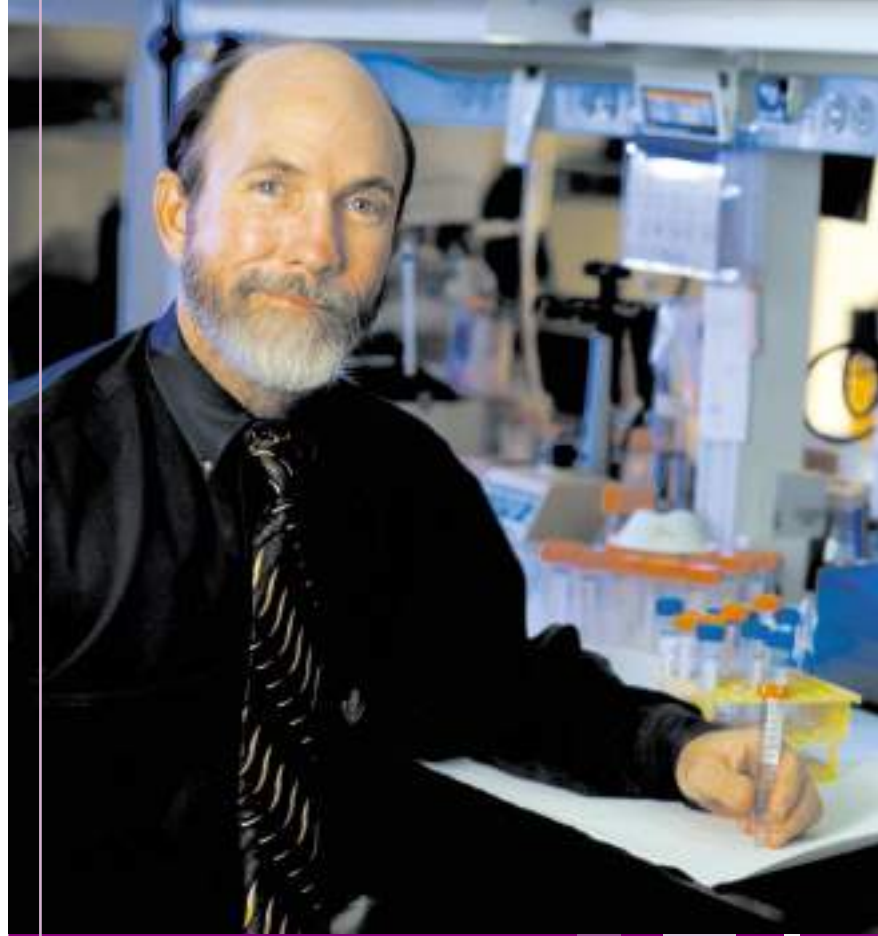
This silent killer also is described as the "silent epidemic," since such a large percentage of the population is infected unawares. An estimated 200 million people worldwide suffer from hepatitis C. In the United States, the virus infects 2 percent of the general population, jumping to rates as high as 4 percent in the 40 – 60 age group and 6 percent or higher in some ethnic groups.

"We all know several people with hepatitis C, even if we don't realize it, because it infects one in 25 U.S. adults between the ages of 40 and 60," said Dr. Robert Lanford, leader of the hepatitis C research program at the Southwest Foundation for Biomedical Research (SFBR) and a member of the National Institutes of Health's Southeastern Hepatitis C Cooperative Research Center.

Challenges in defeating hepatitis C

As elusive as this virus is – unable even to be photographed by an electron microscope – it seems equally challenging to defeat. A difficult, yearlong treatment regimen exists that is 50 percent effective, while the hunt for a successful vaccine to prevent new infections has long seemed impossible because of the virus's divergence.

Hepatitis C virus (HCV) has six different genotypes, or highly divergent groups of viruses, with numerous other strains in each of those genotypes. Researchers and pharmaceutical companies have been trying for years to



Dr. Robert Lanford leads SFBR's groundbreaking research on hepatitis C.

develop a vaccine for HCV, focusing primarily on genotype 1, the most common genotype in the United States and Europe. But there has been serious doubt that an HCV vaccine for one genotype could be effective against the others.

"Concerns have been similar to those about HIV, the virus that causes AIDS, where divergent strains have made vaccine development so challenging," said Dr. Lanford. "But hepatitis C is actually much more divergent than HIV."

New hope – a vaccine is possible

Fortunately, many of those concerns are now being transformed into hope, thanks to recent discoveries by Dr. Lanford and his research team. In 2001, his group was the first to show that chimpanzees that had previously cleared infection with one strain of the virus had protective immunity against a homologous, or similar, strain.

Now, in a February 2004 edition on the *Journal of Virology*, Dr. Lanford, his SFBR colleagues, and collaborators at Johns Hopkins University School of Medicine have provided the first evidence that a vaccine against all strains of HCV should be possible.

Their findings are based on Dr. Lanford's research with chimpanzees at SFBR's Southwest National Primate Research Center. Initially developed by scientists at the National Institutes of Health and SFBR as an animal model for hepatitis C, chimpanzees are the only animals besides humans that can be infected with the virus. As with humans, some chimpanzees maintain chronic infections, while others manage to "throw off," or clear, their infection. However,

Continued on page 8



Helen Lee, a senior research associate in Dr. Lanford's laboratory, develops new tissue culture methods to test hepatitis C drugs.

Hepatitis C, continued from page 7

unlike humans, chimpanzees that remain chronically infected do not develop liver disease. This makes the chimpanzee an extremely important model for vaccine development and testing.

In their research, Dr. Lanford and his colleagues found that chimpanzees that had cleared a previous infection with genotype 1 later showed protective immunity when rechallenged with several different strains of HCV. That was true even when the animals were challenged with a highly complex mixture containing strains from genotypes 1, 2, 3, and 4 – the four major genotypes that affect the vast majority of HCV victims around the world.

Dr. Lanford explained that this finding has significant implications for the eventual development of an HCV vaccine. "This is an important observation, because it means when we are able to make an effective vaccine and immunize a population, people should be protected against all strains of hepatitis C to which they might be exposed," he said. "Until now, there was real pessimism in the research community that cross-genotype immunity could ever be achieved, but this finding shows that it is in fact possible."

Encouraged by this significant discovery, Dr. Lanford nevertheless is quick to point out that an actual vaccine

could be years away. "There is still a major task in front of us," he said. "Although we know a successful vaccine is possible, how do we now go make a vaccine that will induce the same immunity (in an uninfected individual) as is shown by chimpanzees and even some humans who have cleared actual HCV infections?"

Such a vaccine could still be in the planning stages, or it could be one of the new candidates currently under investigation at SFBR. "We're testing new vaccines all the time," said Dr. Lanford. "You never know when the right one will come along."

Search continues for improved treatments

In the meantime, Dr. Lanford's laboratory is testing potential new antiviral treatments for hepatitis C. In collaboration with pharmaceutical companies, new antivirals are being tested for efficacy in chimpanzees as the last step before entering human clinical trials. "We are currently testing four new antivirals in chimpanzees that will probably enter human trials later this year," he said.

Dr. Lanford's laboratory also is conducting research to help scientists uncover new ways to defeat HCV. These studies focus on the differences in the livers of chimpanzees that clear infection with HCV versus chimpanzees that



Chimpanzees have much to teach researchers about hepatitis C infection and how to defeat it.

Facts on hepatitis C

From the Centers for Disease Control and Prevention

What is hepatitis C?

Hepatitis C is a liver disease caused by the hepatitis C virus (HCV), which is found in the blood of persons who have this disease. HCV is spread by contact with the blood of an infected person.

Who is at risk and should be tested for hepatitis C?

- Persons who ever injected illegal drugs, including those who injected once or a few times many years ago
- Persons who were treated for clotting problems with a blood product made before 1987 when more advanced methods for manufacturing the products were developed
- Persons who were notified that they received blood from a donor who later tested positive for hepatitis C
- Persons who received a blood transfusion or solid organ transplant before July 1992 when better testing of blood donors became available
- Persons who have had long-term kidney dialysis
- Persons who have signs or symptoms of liver disease (e.g., abnormal liver enzyme tests)
- Healthcare workers after exposures (e.g., needle sticks or splashes to the eye) to HCV-positive blood on the job
- Children born to HCV-positive women
- Persons who have lived with someone who was infected with HCV and shared items such as razors or toothbrushes that might have had his/her blood on them

maintain chronic infections.

“We’re trying to understand the changes in gene expression that occur in the liver of an animal when it is going through the infection,” he explained. “What happens that allows one to clear the virus and another to remain infected?”

To learn this, Dr. Lanford’s group performs DNA microarray assays, where researchers study the expression of 20,000 genes simultaneously in chimpanzee livers as the animals go through infection. In the process, researchers ask, “Are there differences in the gene expression of animals that clear the infections versus animals that do not? And if so, what changes in liver function or immune response are correlated with those differences?”

“If we could truly understand the difference between a chimpanzee that clears the virus and a chimpanzee that goes chronic, we could develop a successful vaccine and better antiviral treatments for human patients,” said Dr. Lanford.

So, with enthusiasm building from his latest discovery, Dr. Lanford continues his quest to unravel the mysteries of hepatitis C, hoping that future generations can live free from fear of this silent killer.



The extra-uterine development of baby opossums has inspired Drs. Zhiqiang Wang and John VandeBerg to develop unique research initiatives.

Opossum offers promising **new paths for cancer research**



You might not think much about opossums unless you see them crawling along the roadside or perhaps having a late-night standoff with your dog, but these animals could hold the key to exciting new developments in the fight against cancer.

That is the news published this past fall in *Cancer Research*, the nation's most respected cancer journal. There Dr. Zhiqiang Wang, Dr. John VandeBerg and others authored a paper explaining how scientists at the Southwest Foundation for Biomedical Research have developed a unique new animal model for studying human cancers.

The animal is a small South American opossum known as *Monodelphis domestica*, and it is the first animal with an active immune system that has been able to grow cancer cells and tumors from a human. This development opens the door for a host of promising research opportunities, including the

ability to investigate ways to harness a person's own immune system to kill off cancer cells, as well as how the immune system and various chemotherapies work together in this same effort.

Challenges in studying human cancers

Until now, researchers have been limited in how they could study human cancers. Although they could look at naturally occurring cancers in a number of animal models, the only animals that could grow human cancer cells and tumors were mice with immuno-incompetency. In fact, even humans cannot grow cancer cells transplanted from another person, which is why cancer is not a contagious disease. The immune system recognizes those cells as foreign to the body and eliminates them. The reason immuno-incompetent mice can grow human cancers is that they lack the immune system to reject grafted tumors. Even in these mice, however, the cancer rarely metastasizes, or spreads, as it does in people.

New model overcomes previous obstacles

Now researchers have an entirely new and promising path to follow, thanks to the ingenuity of Dr. Wang and his peers. What they have done is capitalize on a unique stage in the opossum's development, a period after the animal is born but before its immune system matures. During this stage, the opossum will accept grafted human tumors, and then those

tumors will continue to grow and even metastasize to other parts of the body after the immune system kicks in. Eventually, though, the immune system fights back, causing the tumors to regress and leaving a healthy opossum.

Researchers say all of these stages of cancer growth and regression will prove helpful in the effort to develop new and improved methods of treatment. For example, the fact that the cancer cells can metastasize in the *Monodelphis* offers several benefits to researchers.

Understanding cancer progression – and barriers to it

“In the *Monodelphis*, we can study what is happening at the molecular level, or in the genes of the cancer cells, that drives the cancer cells to spread,” said Dr. Wang. “If we can discover which genes are responsible for those events, we might be able to devise genetic therapies to block them, thereby halting cancer progression. Likewise, when the cancer starts to regress in the *Monodelphis*, we can search for the genes or immunological markers that are responsible for that regression. This knowledge would assist in the development of new methods for killing cancer in humans, either through genetic therapies or other methods designed to stimulate the desired immune response.”

Harnessing the power of the immune system

In hopes of harnessing an individual’s immune system to fight off cancer, researchers want to study specific antigens produced by the cancer cells as they grow and spread in the *Monodelphis*. Antigens are proteins that are or appear foreign to the body, and Dr. Wang explained that cancer cells produce different proteins during their different stages of growth. “Some antigens go unchecked and escape the immuno-surveillance system, allowing cancer to spread and kill a patient. But because antigens are foreign to the body, they also have the potential to generate a specific immune response that eventually eliminates the material or tissue or cell that carries that antigen,” he said.

He and his colleagues plan to examine the types of antigens produced by the cancer cells in the *Monodelphis* and determine which ones seem to trigger this animal’s successful immune response. “Those antigens might be used as a tool to augment the immune response of a human who has cancer or even to develop possible cancer vaccines,” said Dr. Wang. “Someone might be able to develop a vaccine that uses one of these antigens, so that when a person or animal that has been treated with the vaccine encounters cells with this antigen, their body will recognize it and mount an immunological attack against it.”

He added that improved knowledge of specific antigens and the immune responses they trigger could be useful for

diagnostic purposes as well, helping physicians better screen patients for cancer and even indicating how advanced a person’s cancer is.

Application to individual cancer patients

Dr. VandeBerg is enthused by another valuable opportunity the *Monodelphis* offers, the ability to study how the immune system and various chemotherapies can work together to fight cancer. “A person’s natural immune system plays an important role in the chemotherapeutic process of cancer patients, but until now, we haven’t been able to study these mechanisms side by side in an animal model. So this is really exciting.”

Since different cancers respond differently to different chemotherapies, Dr. VandeBerg said researchers will also



The tiny opossum is helping Dr. Zhiqiang Wang open up new frontiers in cancer research.

want to work with the *Monodelphis* to examine what chemotherapies or combinations of chemotherapies work best against particular kinds of cancer or even against a particular person’s cancer. “I can envision that at some future point we should be able to take cancer cells from a specific patient, grow them in several different *Monodelphis* opossums, and then use different combinations of chemotherapies with the different animals to determine what might be the best method of treatment for that particular human patient.”

Considering all that this small opossum has to offer to human health, Dr. Wang summarizes it like this: “The eventual goal of cancer research is to find ways to kill cancer cells. In the *Monodelphis*, we have a model that can do the work for us. What we need to do now is find out what molecular and immunological events or mechanisms underlie this process and apply that knowledge for human benefit.”

The laboratory opossum:

A small animal with a big impact

t

he successful development of the laboratory opossum as a new model for studying human cancers is one compelling example of this tiny animal's increasing importance to biomedical research – and in turn, to human health.

At SFBR and other research organizations worldwide, the gray, short-tailed opossum, *Monodelphis domestica*, is helping scientists unravel the mysteries of such diverse topics as early development, spinal cord injury and repair, hypercholesterolemia, skin and eye cancers, and even evolution.

This important research and its related advances over the years have been made possible through the leadership of SFBR scientists, with the generous support of local benefactors, in the development and breeding of this unique animal model.

The history

It all started in 1979, when Dr. John VandeBerg, who today is director of SFBR's Southwest National Primate Research Center, made a trip to the Smithsonian's National Zoological Park in Washington, D.C. Having previously worked with captive colonies of large marsupials such as kangaroos and wallabies in Australia, Dr. VandeBerg understood that such large animals were impractical for laboratory research. So he approached the National Zoo with his vision of developing a small marsupial such as the



Dr. John VandeBerg developed the laboratory opossum as a research model. Today, this animal is instrumental to a variety of innovative studies around the world.

Monodelphis as a laboratory animal.

Subsequently, the zoo provided Dr. VandeBerg with 20 first-generation descendants of the nine founders of its own colony. This and an institutional grant from the American Cancer Society allowed Dr. VandeBerg, who at the time was at the University of Wisconsin, to set about the task of discovering feasible methods of care that would keep the animals healthy and thriving in a laboratory environment.

The advantages

This work was painstaking but important to Dr. VandeBerg, who says science was in need of a small marsupial for research: "Since marsupials have very different characteristics from eutherian, or placental, mammals,

particularly in their early stage of birth, my thinking was that any marsupial that could be produced in large numbers in the laboratory would become extraordinarily valuable for research on early mammalian development.”

Explaining this advantage further, he said, “*Monodelphis* mothers produce an extra-uterine fetus, essentially giving birth to their babies at a stage equivalent to a six-week human fetus. This allows you to do some types of fetal development research that you simply cannot do with any other kind of animal.”

Development of worldwide resource

When Dr. VandeBerg came to SFBR as its first geneticist in 1980, he brought with him 28 laboratory opossums and a vision of developing a large resource for scientists at SFBR and beyond. Today, that dream is a reality.

SFBR serves as a world center for research with the laboratory opossum, producing about 5,000 progeny per year – over 70,000 in total since 1980. In addition to maintaining the Foundation’s own fully pedigreed colony of 2,400 laboratory opossums, SFBR makes the animals available to researchers around the globe. Consequently, satellite colonies have been established in other areas of the United States, Canada, Brazil, Australia, and several European countries, making the *Monodelphis* the predominant laboratory-bred research marsupial in the world today.

All of this is possible thanks to generous philanthropic support. Following several years of funding by the National Institutes of Health in the 1980s, strong and consistent grant support from the Robert J. Kleberg Jr. and Helen C. Kleberg Foundation has been used to sustain and enhance the *Monodelphis* colony since 1990. The Kleberg Foundation’s awards have provided for the maintenance of the colony, the continued development of genetic stocks and strains, and pilot studies to utilize this animal’s unique characteristics for new, innovative research applications. In some cases, success with these pilot studies has been used to leverage major new research grants from the NIH.

Captivating work at SFBR

At SFBR, work with the laboratory opossum has followed several interesting paths.

Cancer. Besides the new xenogenetic transplantation work by Dr. Zhiqiang Wang, described on pages 10-11 of this publication, the laboratory opossum is playing an important role in two other areas of cancer research. For one,

Foundation scientists have shown that infant *Monodelphis* exposed to ultraviolet light can spontaneously develop melanoma as adults. This makes the *Monodelphis* the only mammal other than humans known to be susceptible to malignant melanoma as a consequence of UV radiation alone, offering unique opportunities to develop new prevention strategies and to test new treatments for the deadliest form of skin cancer.

The laboratory opossum also is susceptible to a form of corneal cancer induced by UV radiation, and this susceptibility is highly heritable. At SFBR, scientists are studying the genetic mechanisms that contribute to the disease in hope of developing new preventions and treatments.

High cholesterol. In a separate area of research, Foundation scientists have shown the laboratory opossum to be a valuable model for dietary-induced hypercholesterolemia, a major contributor to heart disease. Their studies revealed that a single recessive gene is primarily

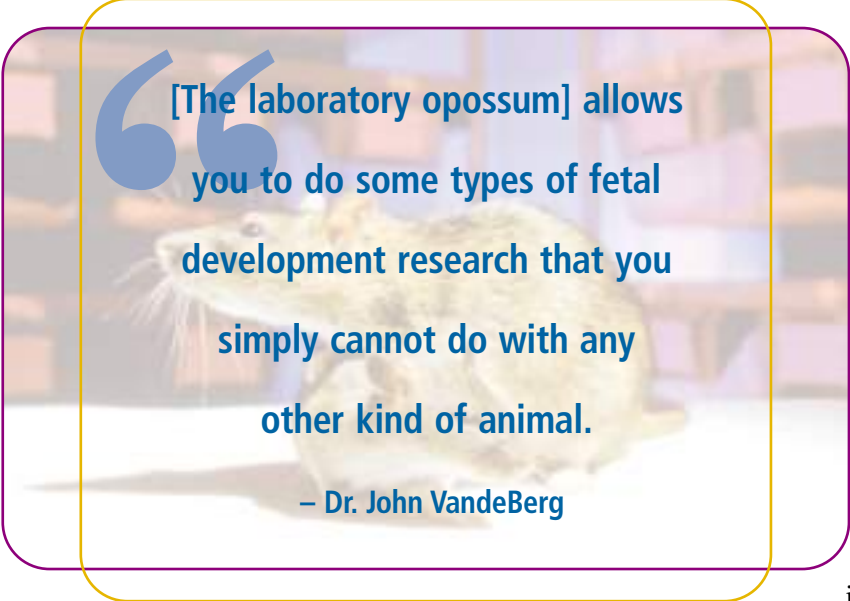
responsible for determining that some opossums are resistant to this condition and others are susceptible. Further investigation is underway to identify the gene and to learn how it functions.

Spinal cord injury and repair. Other fascinating studies – conducted on a small scale at SFBR and to a larger extent at other institutions – are investigating the unique capability of *Monodelphis* to repair severe spinal cord injuries during the first week

of life. Investigators are trying to identify central nervous system genes that switch on or off at this age, rendering the older animals incapable of repairing spinal cord injuries. This work may lead to the development of effective treatments for humans who suffer from these devastating injuries.

Increasing role in genetic research. The importance of the laboratory opossum in biomedical research is expected to grow in light of two recent developments. Under the leadership of Dr. Paul Samollow in the Department of Genetics, SFBR scientists recently developed a first-generation gene map for the *Monodelphis*, which was published in the journal *Genetics* in March. Also, in late 2003, the National Human Genome Research Institute selected the animal as the first marsupial – and one of the few mammalian species – to have its genome sequenced, with work on the project expected to be completed by late 2004. Together, the *Monodelphis* genome sequence and gene map will provide powerful tools for ongoing and future genetic studies.

In these ways and countless others, the laboratory opossum is proving to be a small animal with a big impact on human health.



[The laboratory opossum] allows you to do some types of fetal development research that you simply cannot do with any other kind of animal.

– Dr. John VandeBerg

The 'i' in science

Dr. Andrew Hayhurst works as an engineer for better health



Dr. Andrew Hayhurst's eclectic interests take him from lab work with killer microbes to adventures in the great outdoors.



You recently came to SFBR from the Institute for Cellular and Molecular Biology at the University of Texas at Austin. Part of your work there involved research with an antibody that has proven effective at binding with and inactivating a toxin produced by anthrax. In fact, tests with this anti-toxin have been conducted here at SFBR. What role have you played in this research?

My job has been to find a better, quicker, and less expensive method of producing these antibodies so they can be used as therapeutics. I've done this by generating the antibody molecules in *E. coli*, the workhorse of biotechnology. Just about any lab can use this technology, but the problem is that the antibody needs a chaperone to guide it through the production process. The chaperone helps the antibody fold correctly in *E. coli* into a soluble, and therefore immediately useful, molecule. Without help, the antibody is insoluble and nonfunctional. I've come up with a way of achieving 100 percent solubility so that, in the same amount of time, we can produce 100 or 1,000 times more of these antibodies than we could through other methods, and we can do it much less expensively.

That research must have been exciting, especially during a time that anthrax-laced letters were being mailed around the country.

Absolutely. In a situation like that, it's easy to imagine your work in a research lab being put to good use, and it wakes you up to the fact that we can make the world a safer place through engineering efforts in a biotech lab.

You recently coauthored a paper about an advance in nanotechnology, a new science aimed at making invisibly tiny machines and materials. A Washington Post article described scientists in this field "manufacturing things less than 1,000th the width of a human hair; promising smaller

computers, stronger and lighter materials, and even 'nanobots' able to cruise through people's blood vessels to treat disease." What has been your work in this area, and what did your paper reveal?

Our approach to nanotechnology utilizes "bottom-up" manufacturing rather than "top-down." Instead of taking a chunk of metal and trying to engineer machines to hew that down to infinitesimally small structures, we're trying to take the molecules that form that structure and assemble them from scratch. We can simplify this task by adopting pre-made nanoscaffolds, in our case filamentous virus particles. We genetically engineer the virus to turn the surface of the filament into a "magnet" for molecules, which then deposit themselves in an ordered fashion along the length of the virus filament to form a defined, threadlike shape called a nanowire. In essence, we're minimizing the size of wire.

In the paper I published with Drs. Angela Belcher, Brent Iverson, George Georgiou and others, we explained how we used a particular virus of *E. coli*, M13, as a toolkit for assembling nanowires. M13 is inexpensive to produce and incredibly easy to engineer, so our virus-based toolkit has the potential to replace existing nanomanufacturing processes that can be prohibitively expensive. Right now, we're working on manipulating the length of M13 to allow us to make very long nanowires.

What is the potential payoff of something like this to human health?

If you can imagine technological items being miniaturized and made cheaper and more portable, you can imagine increased applications of computer technology for human health. What if we could miniaturize monitors enough so that they could be used as implants? I'm chasing this with the view that we can push the limits of the system to help create new healthcare tools that until now have only existed in people's dreams.

This is some compelling work you've carried with you from Austin. Haven't you also initiated a new research program at SFBR on SARS?



The chance to work in a BSL-4 lab helped lure Dr. Andrew Hayhurst to SFBR.

I want to come up with diagnostic and therapeutic antibodies to emerging viruses, and right now, SARS is high on the agenda. I have many approaches. Currently, we're using rabbits to generate high-affinity antibodies against the coat protein of SARS. Although these rabbit antibodies would be recognized as foreign to the human body and therefore difficult to use for therapeutics, we can use them as a screening mechanism to detect the SARS virus in a human patient.

Often, the only way to determine if someone has a particular virus is by testing to see if their immune system has produced antibodies to it. However, with many rapid-onset syndromes, infected individuals often don't have time to produce a high enough level of their own antibodies, and physicians are left wondering what, exactly, they have. So a screening mechanism that utilizes rabbit antibodies to detect the SARS virus would be very beneficial for a physician whose patient is showing symptoms that are consistent not only with SARS but also with the flu and other viruses.

How would you go about developing therapeutics for SARS and other emerging viruses?

I am currently creating a library of more than 100 billion different human antibody molecules, from which I will isolate antibodies against emerging viruses. I also want to further evolve some of these antiviral antibodies through genetic engineering methods to combine the strengths of different antibody types found in the human immune response. In that

Continued on page 16

“Nature deals us bigger threats than bioterrorists ever will. I want to help eliminate those threats. – Dr. Andrew Hayhurst



Dr. Andrew Hayhurst revisits his childhood during a trip to the Texas Transportation Museum in San Antonio. Below: He transfers his love for engineering to life-saving work in the laboratory.

Dr. Hayhurst, continued from page 15

way, we can go beyond what the human immune system can do, and we can create more effective antibodies that require lower doses for treatment.

You've done such interesting things at other institutions. What lured you to SFBR?

I've always had an interest in virology, and I still think emerging viruses are our greatest health threat. So after several years working in the more applied field of antibody engineering, I wanted to come back to the field I love and apply my technological skills to combating viruses. SFBR's biosafety level four lab was also a huge pull. There are only a few hot labs in the United States, and this is the only private one. Being here gives me both the physical ability and the academic freedom to study the types of viruses that interest me most.

I understand that working in the BSL-4 has had some unexpected benefits.

It's the only place I was able to overcome my "cedar fever" this winter. I would wake up in the morning blocked up and sneezing, but I'd clear up when I went into the BSL-4, where the air is clean and filtered. It was beautiful. I wanted to stay in there all day.

Allergies don't seem to keep you indoors. Rumor has it you're an avid gardener.

I bought a small house with an acre lot, which right now consists mostly of weeds and mesquite trees. Having inherited my mother's passion for gardening, I'm trying to whip it into shape, and I'd like to start a vegetable garden. My father, who used to brew his own beer, got me into that as well, and eventually I started making my own wine. Now I want to plant hedges of berries so I can bottle wine from my own little

vineyard. I also love to get out and walk in the countryside. I appreciate the nice state parks in South Texas.

Have you always enjoyed hiking, or is that something you've started recently?

I got into trekking when I was a postdoctoral fellow at Aberdeen University in Scotland. The mountains there, which actually are more like high hills, are remote. They make a great place to get away from it all, so I used to take my backpack and disappear into the mountains for days on end. I would ramble from valley to valley with a map, a compass, some food and cooking supplies.

Are there any other interests you developed while living in Europe?

I grew up in London, where my father worked on the railways, first as a platelayer and later as a signal engineer. I acquired his love for railways, and I've long enjoyed building and collecting model railroads. I also like hanging out in old rail yards watching trains go by. It's a wonderful way to revisit my childhood.

You seem to have developed a number of your father's interests.

I share his love for engineering things, but I have to credit my former teachers for my love of biology. Three of my high school science teachers were insanely keen and filled me with such enthusiasm. Then one day I picked up a book on viruses. Near the front was a picture of an ominous black glove holding a test tube with a crystal of poliovirus, and the caption explained how many people the virus could kill. I was amazed that something so small could wreak so much havoc. That drew me to microbiology, and I've loved it ever since. I suppose it works this way with all science, but especially with virology: you never know what's coming next, what virus might soon appear in nature. In fact, nature deals us bigger threats than bioterrorists ever will. I want to help eliminate those threats.



In the spotlight:

SFBR Trustee

Louis Stumberg, Sr.



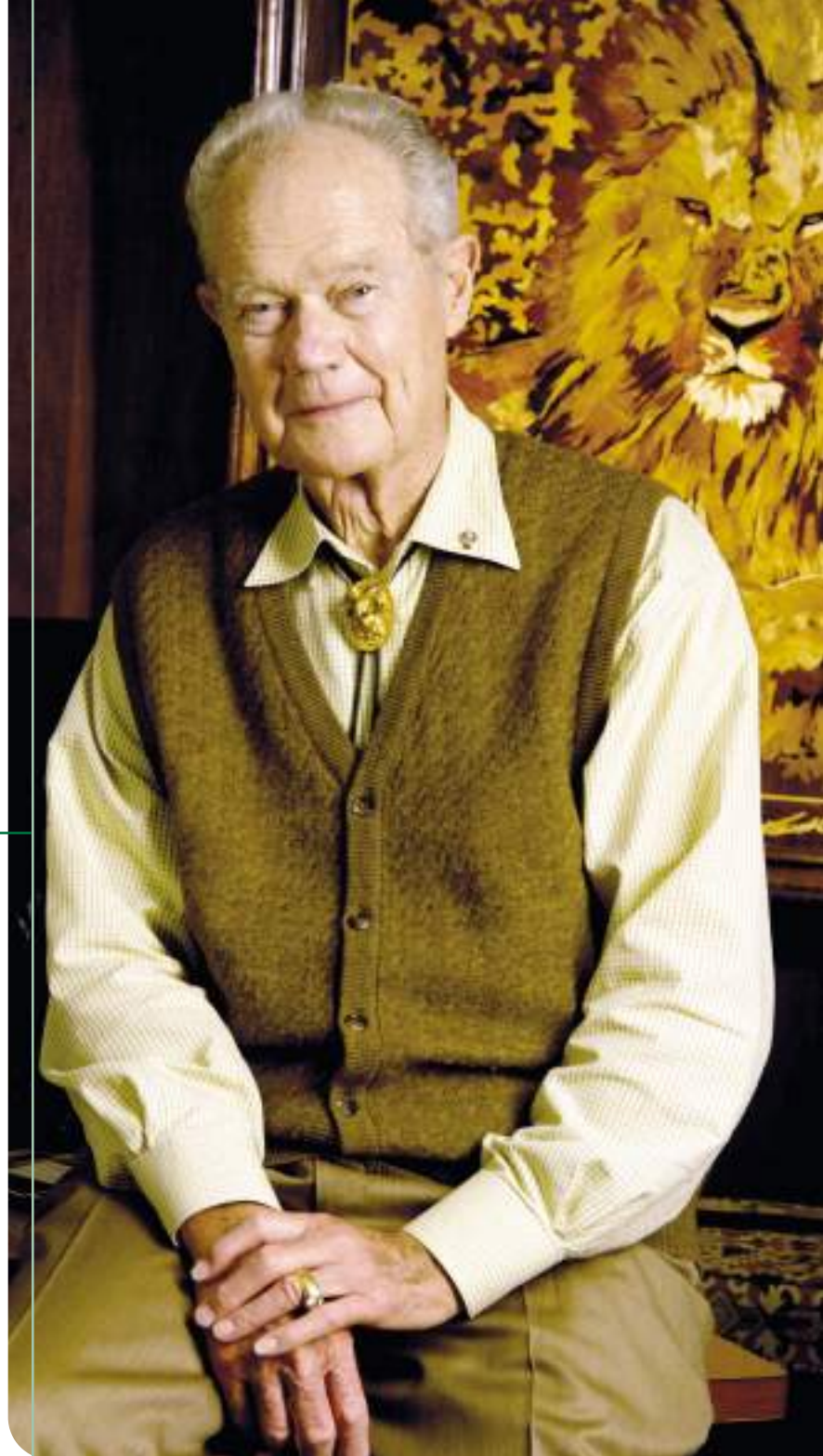
In each issue of Progress, we highlight one of SFBR's stellar trustees. Here our readers have the opportunity to meet Louis Stumberg, Sr., who has long shared SFBR's trailblazing spirit, applying it equally to his business career, personal life and community service.

In San Antonio, the Stumberg family name is almost synonymous with the frozen food business. You were pioneers in developing a market for frozen Mexican dinners, establishing Patio Foods soon after World War II and eventually growing it into an international business. How did that great entrepreneurial idea come about?

My father, brother and I, who founded Patio Foods, didn't share much common ground when it came to business. My father was an electrical engineer, my brother was a geologist, and I had been a mining engineer. After the war, my father in his own unique way said, "Let's start out together in something none of us knows anything about." That's exactly what we did. After considerable thought, we decided to go into the Mexican food business by packing frozen tamales and, at that time, chili, because there was nobody in that business. We spent a year building our plant on Southwest Military Drive, went into operation in January 1947, and over the next 20 years built a company.

What was it like starting from the ground up and trying to create a new market?

I had no training as a salesman and didn't know what I was doing when I first started to approach vendors and brokers about buying our products. I'll never forget the first man I ever called on, Ed Abdo, executive vice president and head buyer for Weingarten's, a large supermarket chain in Houston. I sat opposite him and started trying to sell him Mexican food. He listened to me and then asked, "Mr.



Stumberg, have you ever sold before?" When I told him no, he took the time as a major executive to sit and ask me questions about my product, and when he was through, he said, "If you had told me that, I would have bought, and now that I do know it, I will." For a young man like I was at the time, I couldn't have asked for a better shot in the arm. From him I learned the valuable lesson that, no matter what your position, you must never lose your humanity.

The training he provided in salesmanship also served me well when we decided to branch outside of Texas and go interstate. I traveled around the entire United States opening various markets with brokers, as well as with the U.S. military through its commissaries.

In fact, it was the military that prompted us to venture outside Texas. During the war, so many soldiers had trained

Continued on page 18

Louis Stumberg, Sr., continued from page 17

in Texas or California, where they were exposed to Mexican food and acquired a taste for it. Our aim was to try to recapture their desire for real Mexican food after they moved back to Chicago or New York or Missouri. I had the interesting opportunity of meeting with buyers for the major chains and wholesalers and trying to sell them on foods they had never heard of before. But it was fun, and by the time we'd opened up the entire U.S. market and the military market around the world, we had 76 brokers, all reporting to me. By then I was serving as the company's president, vice president of sales, and vice president of marketing and advertising.

Patio Foods had a number of "suitors" who wanted to acquire it over the years. Why did you finally merge with R.J. Reynolds?

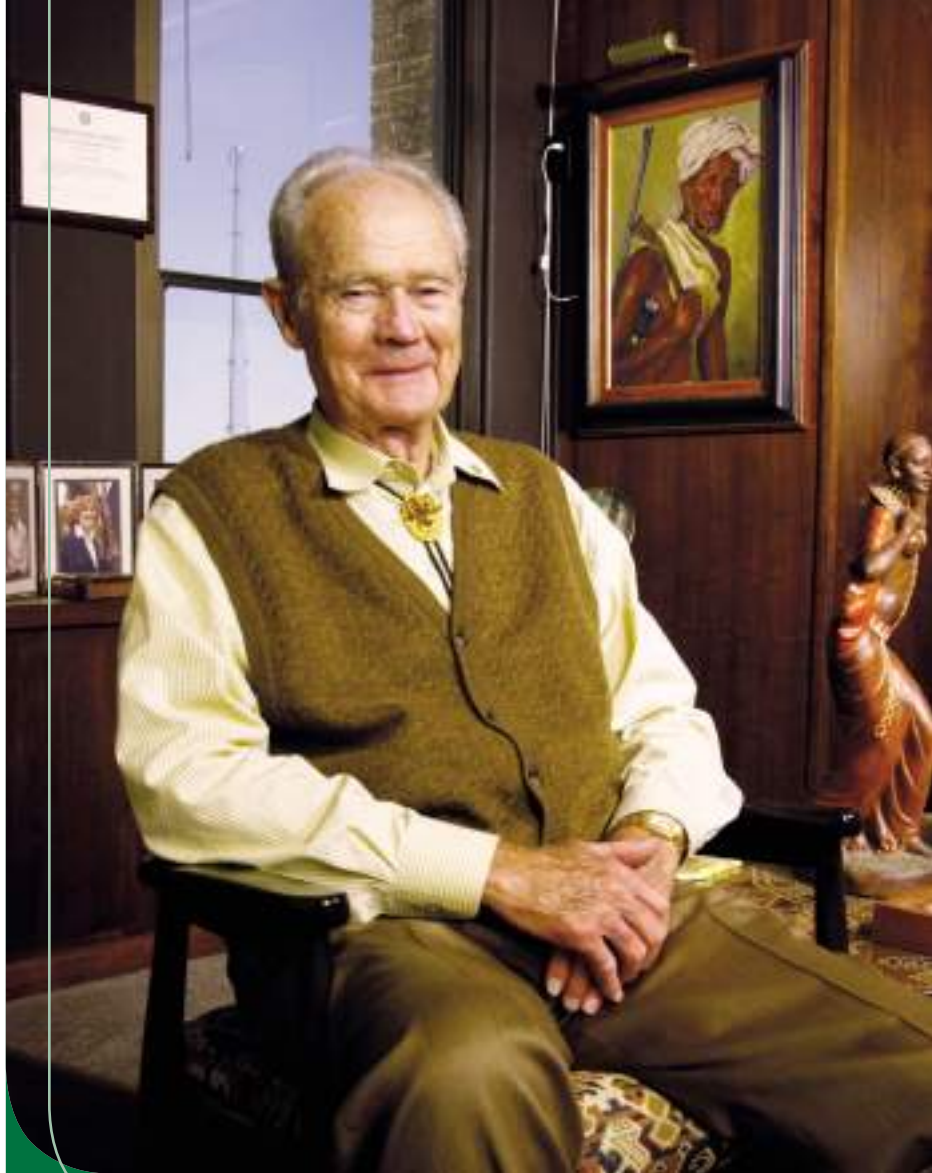
As a family business, we weren't interested in selling, but in October 1966, my father died, and three days later, my son was killed. At that point, I decided I no longer wanted to run a company. We sifted through offers from more than 35 companies, and in July 1967, we merged on a stock purchase with R.J. Reynolds. I became vice chairman of the board of their food operation, and when Reynolds bought Del Monte Foods, I became vice chairman of that board. I spent 20 years with those companies, but I told them from the beginning I wanted to devote part of my time to doing things with my family, in the community and with the state that I wasn't able to do when I was running Patio Foods.

When you said you wanted to get involved with the community, you certainly did. Just a few examples of your leadership include stints as chairman of the Greater San Antonio Chamber of Commerce, mayor of Terrell Hills, member of the Texas Parks and Wildlife Commission, president of the Boy Scouts of San Antonio, campaign chairman for United Way of San Antonio and Bexar County, and president of the Rotary Club of San Antonio. What has been your favorite area of community service?

Each organization has had its own challenges, and each benefits the community in its own way. I've enjoyed working with them all. Actually, I've been trying to cut back in recent years – I've just turned 80 – but it's difficult to do. I'm the longest serving Rotarian in this city, having been with the Rotary Club for 54 years. I was on the board of the San Antonio Zoo for 35 years and the board of Trinity University for 27 years. I'm also the longest-serving active elder at First Presbyterian Church. I guess you eventually get to be the longest-serving member of everything just because you've outlived everybody else.

You also hold the unique position of civilian aide to the secretary of the Army. What does that role involve?

Yes, I've held that position for 13 appointments. Every state has a civilian aide; my appointment just happens to be



Louis Stumberg, Sr.

for a region, the western half of the United States. We interface with the various Army commanders and with the secretary of the Army. They brief us on Army affairs so that if questions come up in our communities, we can answer them. Then of course, they also want our input on behalf of the regions we serve.

For 14 years, I worked for San Antonio to get the new Brooke Army Medical Center (BAMC) hospital. I went to Washington with my brother-in-law, Bartell Zachry, as well as Red McCombs, Gen. Robert McDermott, Dr. John Howe and several others on a number of occasions to lobby for it. Again and again, we thought it was dead, but we finally got it. One time when I was riding with then-Sen. Phil Gramm, I suggested BAMC be renamed the Phil Gramm Lazarus Hospital. When he asked why, I said, "According to the Bible, Lazarus was resurrected from the dead, and if any hospital has been resurrected, it's BAMC, not once but many times. You're the one who called it forth this last time, so I think you and Lazarus should get credit for it." He thought that was hilarious.

I understand that your family also has an interesting historical connection with the military, particularly in Texas.

That's right. My great-great-grandfather was a bugle boy for Sam Houston at San Jacinto. In fact, his bugle and saber were in the Witte Museum for many years.



Whether founding Patio Foods with his father and brother, venturing around the world on safari, or catching a ride on a T-38 Talon, Louis Stumberg approaches life with an adventurous spirit.

“Southwest Foundation shares Tom Slick’s spirit, and that is why I’ve enjoyed being one of its trustees for many years. The Foundation is always reaching out for new frontiers, seeking new cures and better ways to do things. – Trustee Louis Stumberg, Sr.

You seem to share the adventurous spirit of Texas’ early settlers, but you apply it a little differently. Hasn’t your love for hunting taken you around the world?

I’ve made 25 safaris and shikars. My brother and I were two of the first hunters in Afghanistan while it was still a kingdom, and we were the first Americans in Angola. We were the first to hunt in what was then Bechuanaland, now Botswana, and we went on to Mongolia while it was still communist in the 1960s. We’ve also been to Mozambique, India, and a number of other places. Once I shot a lion that was charging my tracker, who was so close that the shot burned the hair off his face. Those trips were exciting, and I’ve loved seeing different parts of the world, but I still enjoy hunting whitetail deer in Texas about as much as anything.

Do you feel like you relate well to SFBR’s founder, Tom Slick, who also shared your adventurous spirit?

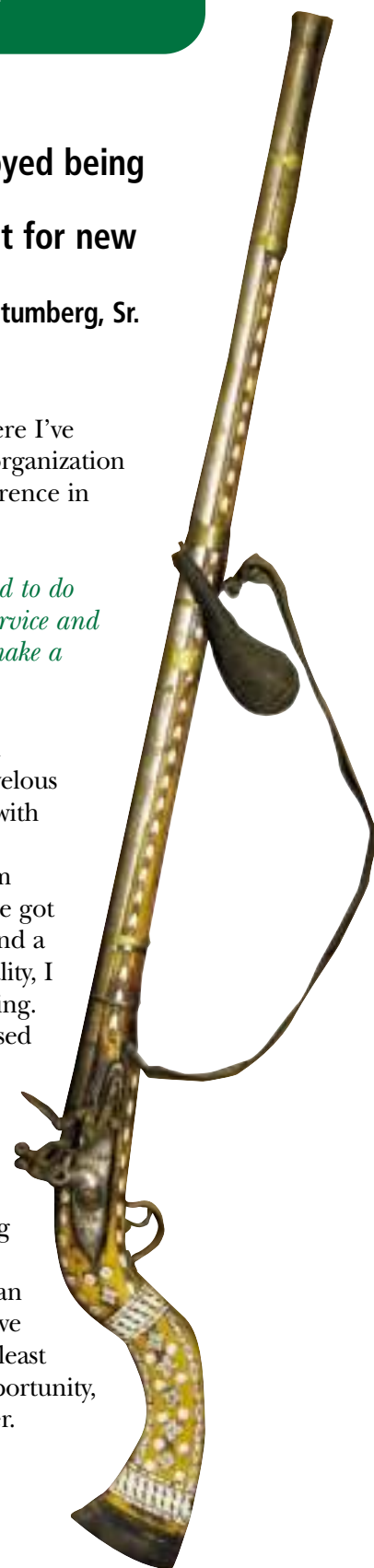
I’m not in Tom’s class. Tom went off searching for the abominable snowman and such. It would have been interesting if he had found credible traces. He is said to have come across hair and other things, but nothing conclusive. I can appreciate, though, why he wanted to do that. His mind was always stretched beyond the horizon. That is the reason Southwest Foundation for Biomedical Research and the Southwest Research Institute exist, because he was such a great visionary – and a fine businessman along with it.

Southwest Foundation shares Tom Slick’s spirit, and that is why I’ve enjoyed being one of its trustees for many years. The Foundation is always reaching out for new frontiers, seeking new cures and better ways to do things. It has so many top-quality people who are doing an enormous amount of good, and oftentimes they’re working on diseases

that came out of areas where I’ve traveled. It’s a marvelous organization that is truly making a difference in people’s lives.

Is that what you’ve tried to do through your community service and generous philanthropy, to make a difference in people’s lives?

I’ve been blessed, both financially and with a marvelous wife of 51 years, as well as with three children and three grandchildren of whom I’m exceptionally proud. So I’ve got a lot to be thankful for – and a lot to give in return. In reality, I don’t believe I’m really giving. Part of what I’ve been blessed with, I’m allowed to keep, and the other part I’m supposed to share. My father taught me that I have an absolute obligation to leave anything and any person I touch as good or in better shape than I found them. Hopefully I’ve had the opportunity, or at least taken advantage of the opportunity, to leave things a little better.





Dr. Henry C. McGill, Jr
Senior Scientist
Emeritus, SFBR

“Golden Circle funds are the most valuable funds SFBR receives because our leadership uses these contributions to start new scientists, support high-risk but promising projects, and assist investigators who face temporary difficulties in the highly-competitive grant game.



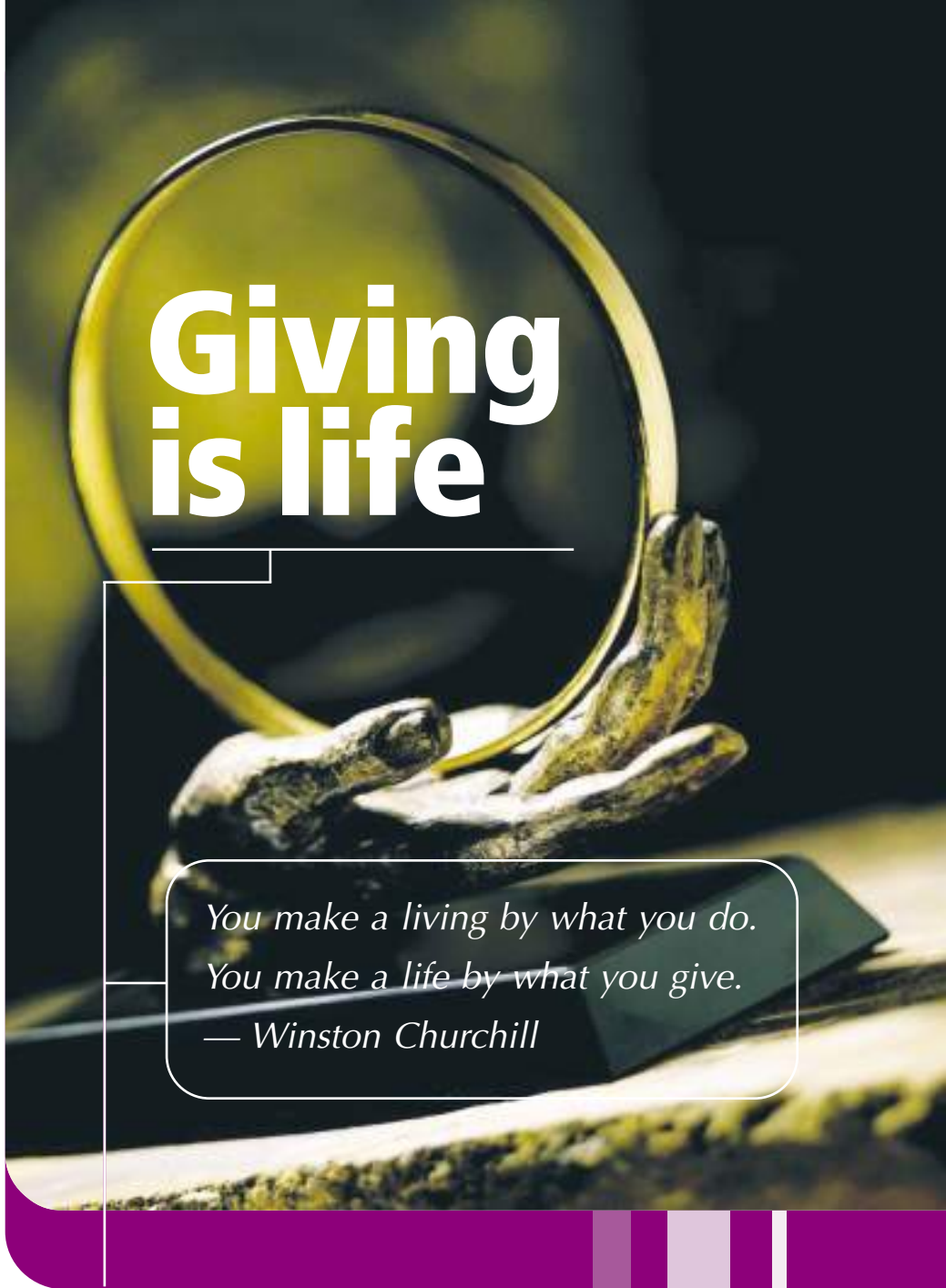
Kaye & B.D.
“Pete” Holt

“We are members of the Golden Circle because we believe SFBR is making a difference in the battle against disease, a difference we could never contemplate achieving on our own.



Kathy &
David
Nicolson

“We have been proud to support this fine organization for over 10 years, and we plan to be a part of the cause for many years to come.



Giving is life

*You make a living by what you do.
You make a life by what you give.
— Winston Churchill*



o give is natural. We give to causes in which we believe. To many, giving is a way to express confidence or shared values.

One of the driving ambitions of humankind has been to understand life and its many forces, including disease and afflictions. It is this drive to understand and unlock life’s mysteries that led to SFBR’s founding in 1941 by an ambitious, philanthropic-minded, 25-year-old Thomas B. Slick, Jr. Contributions from our founder and from our community of supporters have literally built this institution and today sustain many of its operations.

Since the Foundation’s earliest days, philanthropy has played the role of a powerful enabler of progress. Donations, which supplement federal grant monies, also demonstrate to grant-making organizations such as the National Institutes of Health the interest and confidence donors have in the Foundation’s work. This is critical when the granting organization requires matching funds as a condition of its award. In addition, donations may be used to fund scientific salaries, laboratory supplies, equipment and other key research needs, and to fill funding gaps that research grants do not cover. In some instances, donations provide “seed money” for novel and innovative research projects, which are vital to the future of SFBR’s research mission.

You are invited to become a powerful enabler of progress at SFBR

by joining its Circles of Support. Today, would you consider membership in ...

The Golden Circle. The Golden Circle is made up of individuals who give an unrestricted donation of \$1,000 or more annually.

The Corporate Circle. The corporate equivalent of the Golden Circle, the Corporate Circle is made up of corporations who give an unrestricted donation of \$2,500 or more annually.

The President's Circle. This philanthropic giving society includes members who contribute \$5,000 or more to the President's Fund, which is used to purchase needed scientific equipment throughout the year.

The Circles of Support are one of the oldest philanthropic traditions at SFBR. By becoming a member of one of the prestigious circles you become a part of ...

... **a shared vision** of how research can improve life for future generations. Southwest Foundation for Biomedical Research began as the dream of San Antonio businessman and philanthropist Tom Slick, Jr. in 1941. Today, SFBR is one of the leading independent biomedical research institutions in the United States. Our scientists explore the unanswered questions surrounding cancer, heart disease, infectious diseases, neonatal care, lung disease, and genetics, the new frontier of science.

... **a powerful means** to accomplish more through donations than you could typically hope to achieve on your own. Your philanthropic investment in SFBR has more power because it joins with so many others to advance our cause. While SFBR's focus is on basic research into the nature and causes of disease, our work has had significant impact on efforts to develop vaccines, gain insights on human reproductivity, and combat cardiovascular and metabolic diseases, cancer, and lung disease of the premature infant.

... **the home institution of some of our country's most productive researchers.** SFBR researchers are among the most productive by any measure. On average, for every \$1 contributed, SFBR scientists gain another \$8 in competitive grant support, making our researchers among the most productive anywhere.

... **a home for many extraordinary resources** that encourage collaboration among SFBR researchers and their colleagues from every corner of the world. SFBR has a history of developing rare scientific resources. The SBC Genomics Computing Center, the neonatal intensive care research center and the BSL-4 maximum containment laboratory are examples of such resources funded by donations.

Invest in the Future

Like Tom Slick's initial vision for the Foundation, our continuing success depends on the dedication and commitment of our corporate and private philanthropists, combined with our scientists' aggressive pursuit of competitive funding to underwrite research programs. Your donation is an investment in this pursuit of a healthier tomorrow for each of us through superior biomedical research.

To make a donation to one of SFBR's Circles of Support, contact Corbett Christie, SFBR's chief development officer, at (210) 258-9870, or simply fill out and return the form on the right.

Join SFBR's Circles of Support

I wish to join the Circles of Support:

(Check one)

New member

Renewing member

(Check one)

Golden Circle \$1,000

Corporate Circle \$2,500

(Individuals only)

President's Circle \$5,000

Please type or print clearly, as this is how the name(s) will be printed in our publications.

Personal information for Golden Circle and President's Circle memberships

Name _____

Address _____

City/State/Zip _____

Home telephone number _____

Personal e-mail address: _____

Professional information for Corporate Circle memberships and for organizations that would like a President's Circle membership

Company name: _____

Contact name: _____

Work address: _____

City/State/Zip _____

Work telephone number _____

Work e-mail address: _____

May we list your name in our publications? Yes / No

Payment method

Enclosed is a check for \$ _____ made payable to SFBR.

Please bill me quarterly/annually (circle one) for a total of \$ _____

Please charge my credit card for my donation in the amount of \$ _____

Card type:

MasterCard

Visa

Discover

American Express

Credit card #: _____

Billing address: _____

Would you like us to send you an annual reminder to renew your membership? Yes / No

Mailing instructions

We will send you information on the giving level you have selected along with a receipt for tax purposes. Please mail your check to the following address:

SFBR Development Office

P.O. Box 760549

San Antonio, Texas 78245-0549

Thank you for including SFBR in your giving plan. For more information on naming SFBR in your will, on leaving a gift from your trust or foundation, or on gifts to name a building or laboratory, please call Corbett Christie, chief development officer, at (210) 258-9870.



Southwest Foundation Forum

Spreading the 'good news' about SFBR



Ladies of the Southwest Foundation Forum have taken their community relations mission to heart, hosting a wealth of recent activities to share SFBR's positive story with members and the public.

In November, there was not a spare seat to be had at the popular Fall Lecture Luncheon. The event drew a record-setting crowd to hear SFBR virologist Dr. Rebeca Rico-Hesse, who described her research with emerging viruses that threaten to cross the U.S. border.

Throughout the winter and early spring, high school students were beneficiaries of the Forum's outreach activities. Students from 10 area schools participated in Forum-sponsored tours of SFBR, which included an overview of the Foundation's research programs, a tour of its extraordinary nonhuman primate colony, and interaction with one of SFBR's top scientists. These visits gave the students a unique opportunity to learn about scientific research as well as its valuable career opportunities.



Forum members and their guests from other SFBR support groups enjoyed their own, moonlit tour of the Foundation on the evening of March 10. Following a delightful cocktail buffet and reception, guests walked the grounds of the SFBR campus to tour its facilities and engage in conversation with SFBR scientists. First-timers and annual attendees alike said the event was a wonderful way to learn about the life-saving research programs they support throughout the year.

On March 24, the Forum's focus returned to high school students once again as the group's Spring Lecture Luncheon hosted the winners of their Science Education Awards. Each year, the Forum and the V.H. McNutt Memorial Foundation join together to award grants for innovative high school science projects. This year's winning applications were from two classes at Samuel Clemens High School and one class with the Cibolo Alternative Program. Congratulations to all on a job well done.

A sell-out crowd attended the Forum's Fall Lecture Luncheon to hear Dr. Rebeca Rico-Hesse (top left) describe her research on emerging viruses.

Would you like to be a part of Southwest Foundation Forum and its worthy efforts? Contact Brooke Connolly, Forum vice-president for membership, at (210) 828-4600 or brooke@connollycompany.com.



Forum members and guests enjoyed an evening tour of SFBR with Foundation scientists.



The Founder's Council

Monumental ending to 2003...

The Founder's Council, which enjoyed a monumental closing to the 2003 year, has jump-started 2004 with contagious enthusiasm.

On Dec. 10, 2003, more than 240 members and guests gathered at the beautiful home of the late Robert Tobin to celebrate the group's 15th anniversary and annual holiday party. On this grand occasion, Council founders Bruce Bugg and Jim Gorman played a special role in the evening's festivities as the group distributed a record-setting \$25,000 in grant awards to SFBR scientists in support of their research.

The highlight of the evening was the awarding of the Albert Steves IV Memorial Grant to Dr. Robert Lanford, scientist in SFBR's Department of Virology and Immunology, for his groundbreaking research on hepatitis C. The Founder's Council worked with the late Albert "Aboo" Steves' wife, Martha Monier Steves, and her family to establish the grant after Aboo passed away in February 2003. As director of special projects for SFBR, Aboo assisted the Founder's Council from its inception, offering the group his guidance, direction, and valuable support.

With the help of more than 100 friends and family members, the Founder's Council has, to date, raised more than \$35,000 for the memorial fund, which will allow the group to make this new grant its lead annual gift. Martha Steves and her children Albert Steves V, Kurt Monier Steves and Francie Steves Calgaard were honored at the celebration and helped President Bob Shemwell present the inaugural grant.

Other grants awarded that evening went to Dr. Nicolas Gouin for his cancer research; Helen Martin to support SFBR's research into new therapies for diseases of the premature newborn; Dr. Susan Mooberry for her cancer drug discovery program; Dr. Krishna Murthy to support his tests on candidate vaccines for HIV; Dr. Qiang Shi, a geneticist who is studying factors that contribute to heart disease; and Dr. Paul Zhou, who is developing therapies against cancer and HIV.

A special thank you goes to the Tobin Endowment for underwriting this extraordinary event.

... leads to enthusiastic beginning for 2004

Enthusiasm from the holiday party carried over to the Founder's Council speaker luncheon on Feb. 25, when members heard first-hand how their grant award to Dr. Robert Lanford is making an impact. Dr. Lanford explained his latest findings on hepatitis C, the leading cause of liver failure in the United States. To learn more about his efforts to defeat this "silent killer," see the full story on pages 7-9 of this publication.



Founder's Council President Bob Shemwell and Martha Steves present the Albert Steves IV Memorial Grant to Dr. Robert Lanford.



Recipients of the Founder's Council 2003 grant awards were (L-R): Dr. Susan Mooberry, Dr. Paul Zhou, Dr. Krishna Murthy, Dr. Nicolas Gouin, Dr. Robert Lanford, Helen Martin, and Dr. Qiang Shi.



Honored at the holiday party were family members of the late Albert Steves IV: (L-R) Kurt and Amy Steves; Kent and Francie Calgaard; Martha Steves; and Tricia and Albert Steves V.

For membership and other information about the Founder's Council, contact Amy Abdalla at (210) 258-9409 or amy@sfbr.org.

Honor a loved one with a gift for the future



"Laboratories are
sacred places where
the future is born."

– Louis Pasteur

There are many ways to honor our friends and loved ones, but none as lasting as a gift that impacts the future. A memorial or special occasion contribution to the Southwest Foundation for Biomedical Research is just such a gift.

In the laboratories at SFBR, scientists are working to unlock the mysteries of biological science, advancing the development of preventions and cures for the diseases that plague our world. Their explorations delve into the unanswered questions surrounding cancer, heart disease, infectious diseases, neonatal care, lung disease, and genetics, the new frontier in science.

By choosing to support these life-saving efforts of SFBR scientists, you can have an impact on the health and happiness of people today and for generations to come.

Your donation might serve as a lasting remembrance of a loved one or as an expression of congratulations for a happy milestone event. Whatever the occasion, you will be helping SFBR create a brighter future through research into the detection, cause, prevention, cure, and eradication of disease.

Have you thought of these opportunities for honor gifts?

Birthday
Birth of a child or grandchild
Anniversary
Graduation

Get well wishes
Holiday greetings
Expression of thanks
Congratulations for
awards or achievements

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!**

About Southwest Foundation

a

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

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

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

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

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



advancing human health
today.

Non-profit Organization
U.S. Postage
PAID
San Antonio, Texas
Permit No. 958



P.O. Box 760549
San Antonio, Texas 78245-0549