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SFBR launches its first spin-off company

Drug development venture built around life's work of Senior Scientist P.N. Rao

Inside

Message from the President

John C. Kerr

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In its own version of *Back to the Future*, this issue of *Progress* takes readers on a thrilling journey, as we see how the Foundation's rich history and the efforts of various individuals over previous decades have enabled the scientific success we're enjoying today, and how they've positioned the Foundation and the city of San Antonio for even greater achievement in the future.

Consider Dr. P.N. Rao , who came to the Foundation in 1958, when he and his colleagues had to work in a farm building converted to laboratory space. With that rather shocking and humbling start to his career here, he embraced the bold vision of SFBR founder Tom Slick, with whom he quickly became friends, and became a world leader in the field of steroid chemistry. Today, he holds 17 patents in steroid hormone synthesis and immunoassay methodologies that have had a marked impact on physicians' abilities to diagnose and effectively treat reproductive disorders and various forms of cancer. And at a point in his career when most people would retire, he is playing a key role in the establishment of SFBR's first spin-off company, Evestra Inc.

With a highly impressive leadership team that includes the former chief operating officer of ILEX Oncology, Dr. Ze'ev Shaked, Evestra is in fact being called by some "San Antonio's next ILEX." That remains to be seen, but as Evestra builds upon the accomplishments and expertise of Drs. Rao, Shaked, and other key leaders, it has the potential to be an industry leader in the area of women's health and cancer treatment, a great financial investment for SFBR, its largest stakeholder, and a vital new component of San Antonio's increasingly robust bioscience industry.

Another visionary idea embraced by SFBR trustees and donors in its recent history was the construction of a state-of-the-art virology complex that includes the nation's only privately owned BSL-4 laboratory. This extraordinary resource has allowed SFBR to develop world-class research programs in the areas of biodefense and emerging infectious diseases, including a new collaboration with SRI International to test existing FDA-approved drugs for the ability to treat bio-threat agents.

It's also a vital resource in a citywide effort to bring the first major federal research laboratory built in the last 50 years to San Antonio. The National Bio and Agro-Defense Facility, or NBAF, will be a $450 million federal installation to address national biological and agricultural security risks, and it will be a boon to whichever city is chosen to host it.

Thanks to the united effort of numerous local organizations, including SFBR, San Antonio is a strong contender among the five U.S. cities that remain in competition for the NBAF. In fact, SFBR's unique experience and expertise in maximum-containment research is something that sets San Antonio apart from its competitors. SFBR is happy to be a major supporter of the local effort to win the NBAF, which if successful would represent the single most important new development in a 20-year effort to promote the biosciences in San Antonio.

Another extraordinary resource at SFBR has its origins in the 1950s, when scientists first discovered that the baboon was a natural model for the study of atherosclerosis and other aspects of cardiovascular disease. Today, the Southwest National Primate Research Center is one of SFBR's crown jewels, enabling innovative and groundbreaking studies by investigators at SFBR and around the world. It also has helped attract luminary scientists to key positions at our organization, including Dr. Thomas Folks, who recently came to the SNPRC after a distinguished career at the Centers for Disease Control and Prevention. *Progress* readers should enjoy learning about his outstanding accomplishments in public health efforts to detect and identify emerging viruses and to prevent the spread of HIV. As you do, you will see why we're thrilled to have him as part of the SFBR team.

Other scientific highlights in this issue include the discovery by Dr. Robert Shade and his local and international colleagues of the area of the brain that is responsible for a decreased sense of thirst in the elderly – a finding that could lead to treatments that would renew a proper sense of thirst and decrease the risk of dehydration among the elderly. And Dr. Joanne Curran, a bright young scientist in our Genetics Department, is building upon previous findings by her and several other SFBR scientists as she uses a new federal grant to look more closely at the top 100 genes that SFBR studies have shown to influence diabetes risk factors.

Finally, I believe our readers will enjoy a trip through SFBR history with J. Burleson "Burley" Smith, who has served as a trustee nearly since the Foundation's inception. After World War II, he returned to San Antonio to join a new law firm that was the predecessor to today's Cox Smith Matthews Inc., and in the process, became closely involved with the Slick family and the fledgling research institution founded by Tom Slick. As one of the cornerstones in our foundation, Burley Smith knows from firsthand experience just how far SFBR has come and the potential we have for even greater achievements in the future.

SFBR launches its first spin-off company

Evestra Inc. drug development venture built around life's work of Senior Scientist P.N. Rao

When Genzyme Corp. paid $1 billion for San Antonio-based ILEX Oncology in 2004, a longtime vision of many of the city's business and civic leaders was realized. Those who had long before dreamed of San Antonio becoming a serious player in the bioscience business saw the big-dollar purchase of the homegrown ILEX, a spin-off of the Cancer Therapy & Research Center in the mid-1990s, as a major milestone. The city had, indeed, stepped onto the world stage in a new and exciting way.

John Kerr, president of Southwest Foundation for Biomedical Research, is not suggesting such a massive pay-off is in the offing, but he's undeniably excited about SFBR launching its first spin-off company, Evestra Inc. Here's how Kerr, who first envisioned the Evestra concept, describes the new company:

Incorporated in late 2007, Evestra is receiving all of the assets, personnel, and scientific know-how of the Foundation's Organic Chemistry Department, an internationally recognized research group in steroid chemistry, together with start-up funding from SFBR, which will initially be the majority shareholder of the new company. In addition to funding provided by SFBR, Evestra is raising an initial round of financing primarily from San Antonio-area investors.

Evestra is being built on the department's 30-plus years' experience in the discovery and synthesis of novel steroid compounds used in a wide range of female healthcare applications, including contraception, gynecological diseases, hormone replacement therapy, and hormone-dependent breast cancer.

Dr. P.N. Rao, the distinguished chair of the department, is teaming with Dr. Ze'ev Shaked, the former chief operating officer and head of R&D at ILEX, who will serve as president and CEO of Evestra, and with Dr. Klaus Nickisch, the former senior vice president of Schering AG in Germany, who will serve as Evestra's chief scientific officer. Both Drs. Shaked and Nickisch hold Ph.D.s in Organic Chemistry.

By combining SFBR's steroid synthesis capabilities with the extensive drug development track record of Evestra's management, Evestra is commercializing a pipeline of products in fertility control, hormone replacement therapy, and oncology.

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"Over the past 50 years at SFBR, Dr. P.N. Rao has been one of the world's foremost experts on steroid chemistry and women's fertility and cancer," said Kerr. Dr. Rao, who became chairman of the Organic Chemistry Department in 1977, later was given the Foundation's highest honor, being named "Senior Scientist" and receiving from the Board of Trustees the Maltese Cross, symbolic of intellectual acuity. "The lifetime body of work he has created and the incredible breadth and depth of his knowledge are invaluable assets to Evestra," Kerr added.

"Dr. Rao and his team's superb record in designing and synthesizing novel steroids has been recognized by the National Institutes of Health and by his peers around the world," said Dr. Shaked. "So the spin-off of his department into Evestra, especially when combined with the experience of the management team that's in place, creates a truly exciting opportunity."

Dr. Shaked said the company has the scientific know-how, the leadership, and the experience in the steroid world that are needed to "hit the ground running. That allows us immediately to execute our business plan based on the development and commercialization of steroid-based pharmaceuticals, giving Evestra great potential for success. And as Evestra becomes successful, that will benefit SFBR, as well as the San Antonio community."

The pipeline

Evestra is pursuing a capital-efficient short-term and long-term drug development strategy. The short-term strategy is based on the reformulation of existing, approved steroid-based pharmaceutical products. The long-term strategy involves the in-house development of novel steroidal drugs based on the expertise of its organic chemistry team.

The leading drug candidate, a reformulated oral contraceptive, involves seeking an accelerated approval from the FDA. Four additional drug development candidates support the company's strategy of having "multiple shots on goal" – think of a soccer team shooting at the goal five times instead of just once – to increase the odds of success.

In addition to the leading candidate, the Evestra team also is working on:

- Developing novel progestin drugs for fertility control
- The reformulation of a hormone replacement therapy with a superior safety profile
- Finding a new drug candidate for endometriosis and fibroids
- Developing new drugs to prevent the recurrence of breast cancer

Along with its primary focus of developing a solid pipeline of pharmaceutical products, Evestra will generate revenue from the synthesis of steroids for the National Institutes of Health pursuant to a contract SFBR has had for over 30 years, which is being transferred to Evestra.

The team

SFBR has assembled a true leadership powerhouse to ensure the success of this new venture. Evestra will benefit from the great depth of scientific and corporate expertise of its management and board:

A powerful leadership team has come together to launch the SFBR spin-off Evestra Inc. Some of the team's key members meeting here are Dr. Klaus Nickisch, chief scientific officer and managing director, Evestra-Germany; SFBR President John Kerr, who first envisioned the Evestra concept and is now a member of the Board of Directors; Dr. Ze'ev Shaked, Evestra president and CEO; and Dr. P.N. Rao, Evestra's senior vice president of research.

SFBR's Organic Chemistry Department, renowned for its expertise in steroid synthesis, is being transferred to Evestra Inc. as part of an exciting new business venture. The department team includes (L-R) Baishaki Das, James Cessac, Kirk Acosta, Chairman P.N. Rao, and Martin Bahr. Not pictured is Anne Marie Simmons.

Ze'ev Shaked, Ph.D. – President and CEO. Before founding Evestra, Dr. Shaked was chief operating officer of ILEX Oncology and president of ILEX Products Inc. and held a number of senior R&D and management positions with other pharmaceutical companies, including Spherics Inc., ImmuLogic Pharmaceutical Corp., Berlex Biosciences Inc., Triton Biosciences Inc., CODON Corp. and Chiron Corp. He has extensive experience in the development of biologics and conventional drugs.

Klaus Nickisch, Ph.D. – Chief Scientific Officer and Managing Director, Evestra-Germany. Dr. Nickisch spent over 28 years with Schering AG, one of the leading international pharmaceutical companies, in a wide range of positions before the recent merger of Schering with Bayer. Beginning as a medicinal chemist, Dr. Nickisch moved from research to product development and project management, leading a number of major programs in oncology and female healthcare and finally serving as senior vice president and head of global project management.

P.N. Rao, Ph.D. – Senior Vice President of Research. Dr. Rao joined SFBR 50 years ago and has served as chair of its Organic Chemistry Department since 1977. He holds 17 patents in steroid hormone synthesis and the immunoassay methodologies that have had a marked impact on physicians' abilities to diagnose and effectively treat reproductive disorders and various forms of cancer. He and his research team also have made significant contributions in the development of novel steroid hormones that inhibit the action of progesterone, which plays a major role in breast and ovarian cancer and endometriosis. Proellex™, a drug his team developed at SFBR in collaboration with the NIH and licensed to a Houston-based company, Repros, is currently undergoing late-stage human clinical trials and showing great promise in treating endometriosis and shrinking fibroid tumors without surgery. Other steroid compounds synthesized and patented by Dr. Rao have shown significant anti-cancer activity by interfering with the blood supply to the tumor, with potential application to the treatment of breast and prostate cancer.

The Evestra Board of Directors consists of Kerr, J.R. Hurd, chairman of the SFBR Board of Trustees, Dr. Shaked, and Dr. Nickisch.

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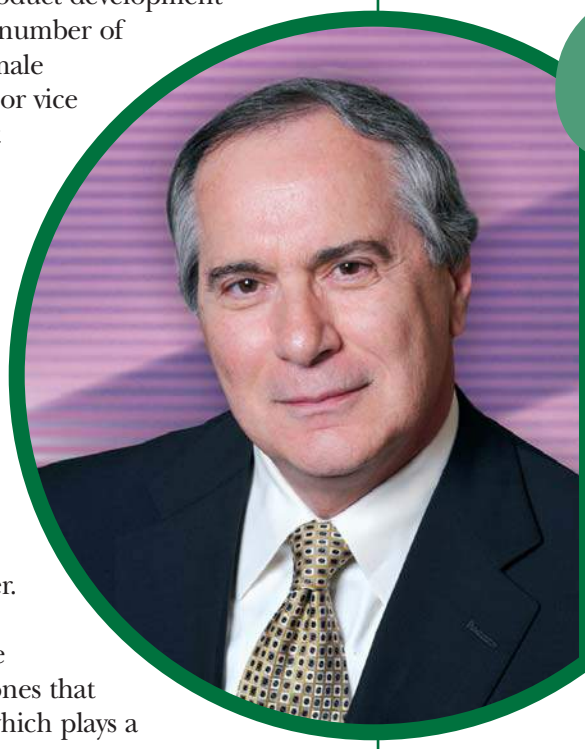

"As Evestra becomes successful, that will benefit SFBR, as well as the San Antonio community."

— Dr. Ze'ev Shaked, President and CEO of Evestra Inc.

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Evestra also boasts an impressive Scientific Advisory Board. Chaired by Dr. Nickisch, its other members include Dr. Rao and a team of experts from the United States and abroad:

- Walter Elger, M.D. – Former head of Female Health Research, Schering AG and Jenapharm
- Irving Spitz, M.D., Ph.D. – Director of the Institute of Hormone Research in Jerusalem, emeritus professor of endocrinology at Ben Gurion University in Israel, and adjunct professor of medicine at Weill Medical College of Cornell University
- Werner Raff, M.D. – Former head of Female Health SBU, Schering AG
- James W. McGinity, Ph.D. – Professor and division head of Pharmaceutics, College of Pharmacy, University of Texas at Austin
- Robert Shenken, M.D. – University of Texas Health Science Center at San Antonio, chair of the Department of Clinical Gynecology

"One rarely sees a new company being formed with such an impressive scientific and management team," said Kerr. "Truly, each of these men is world class in his own right. Their coming together for this new venture presents us with a tremendous opportunity to build a company that will be an industry leader in the area of women's health and cancer treatment."

Kerr continued, "That's exciting for San Antonio, and it's exciting for the Foundation. The spin-off of Evestra advances our mission to improve human health through innovative biomedical research, and it could ultimately be of tremendous financial importance to SFBR, its largest stockholder, as the value of its holdings increases."

Looking back on his 50 years' work and forward to the future of Evestra, Dr. Rao had this to say, "It's gratifying to see the potential of the work we've done in reproductive health. By commercializing this work, we may be able to improve the lives of people in all parts of the world and at the same time produce a financial dividend for SFBR that will support this great institution's research for many years to come. I'm honored to be a part of it."

"Truly, each of these men is world class in his own right. Their coming together for this new venture presents us with a tremendous opportunity to build a company that will be an industry leader in the area of women's health and cancer treatment."

– SFBR President John C. Kerr

Drs. P.N. Rao and Klaus Nickisch discuss one of Evestra's initial drug development projects.

SFBR is partnering with other local institutions to help bring a new federal laboratory to San Antonio.

National Bio and Agro-Defense Facility could be a game changer for San Antonio

Texas is full of cities that were transformed by a single, game-changing event into powerhouses in various industries. NASA landed in Houston, and to this day the "Bayou City" is the epicenter of space travel. Dallas and Fort Worth were essentially forced to work together to develop a regional airport, but it is now among the busiest in the world. Austin beat 56 other cities competing to land the Microelectronics & Computer Technology Corp., or MCC, and suddenly was seen by the world as a major high tech hub.

The National Bio and Agro-Defense Facility (NBAF) has the potential to have a similar impact on San Antonio.

SFBR stands among the strongest supporters of San Antonio's effort to win NBAF, a $450 million federal installation that will conduct research and testing on infectious diseases that threaten agricultural animals or that can be spread from animals to humans, including certain bioterrorism agents.

Five sites nationwide, including San Antonio's Texas Research Park, are under consideration by the U.S.

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San Antonio's proposed site for the NBAF

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Department of Homeland Security (DHS) as the site for the 520,000-square-foot NBAF. The NBAF would replace the aging Plum Island Animal Disease Center research complex at Plum Island, N.Y., and expand its size and scope. With the terror attacks of Sept. 11, 2001, and the anthrax-laced mailings that followed that same October, the threat that terrorists might use biological weapons to attack the U.S. population directly or through the agricultural industry became all too real. In addition, the spread of West Nile virus across the United States and outbreaks of emerging viruses such as SARS and avian flu have brought home the threat of diseases that might naturally spread from animals to humans.

For these reasons, the NBAF is intended to enhance our nation's capacity to respond to threats against both humans and animals. That includes Plum Island's original focus on foreign animal diseases such as foot-and-mouth disease as well as zoonotic diseases, or those diseases that can transmit from animals to people.

Who is competing for the NBAF?

When the DHS announced its intention to build the NBAF in 2006, San Antonio formed a consortium consisting of SFBR, the Texas Research and Technology Foundation, the University of Texas Health Science Center at San Antonio (UTHSCSA), the University of Texas at San Antonio (UTSA), and Brooks City-Base to compete for the federal lab. The consortium, known as the Texas Biological and Agro-Defense Consortium, or TBAC, proposed three sites in San Antonio for the NBAF, one at SFBR, one at the Texas Research Park, and one at Brooks City-Base. In July 2007, DHS announced a short list of five sites nationally under consideration for the NBAF, including the Texas Research Park site.

The other sites on the short list competing with the Texas Research Park are:

- Flora Industrial Park, Madison County, Miss.
- Kansas State University, Manhattan, Kan.
- Umstead Research Farm, Granville County, N.C., and
- University of Georgia, Athens, Ga.

All of the sites have been undergoing review for the required federal Environmental Impact Statement, a draft of which is expected this summer, followed by a final EIS this fall. DHS has indicated that it will announce its final decision on the NBAF site selection in October. However, construction of the facility will be dependent upon an appropriation by Congress.

How would the NBAF benefit the Alamo City?

In addition to providing numerous construction jobs while being built, the NBAF would bring to San Antonio at least 300 lab-related jobs, officials have said.

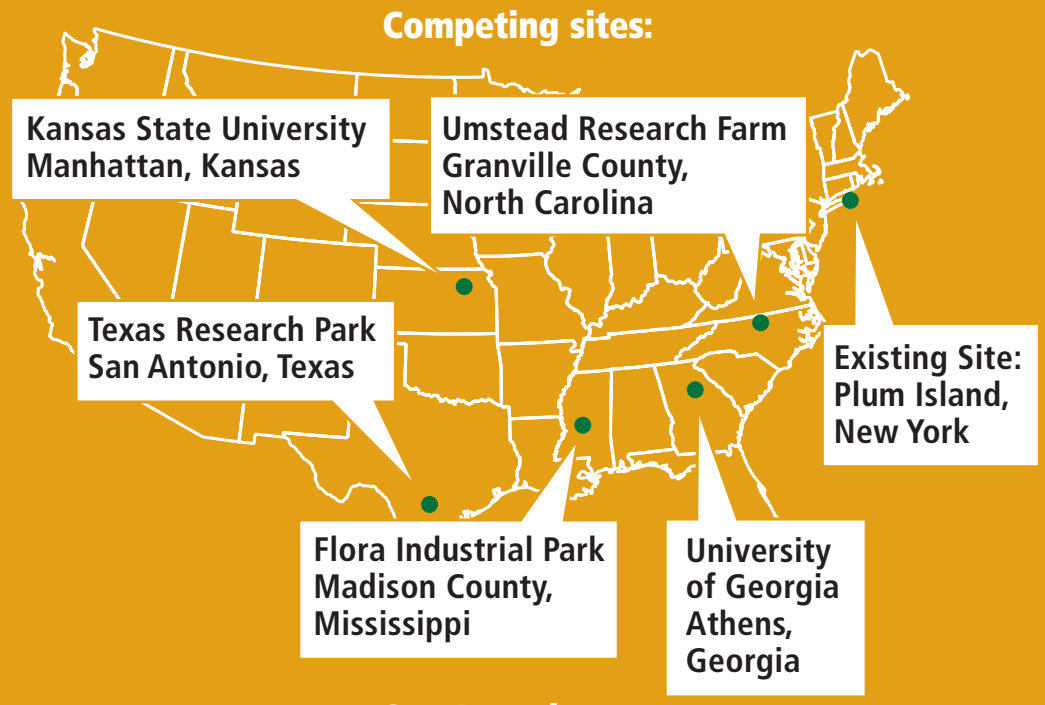
"SFBR strongly supports the local effort because it would benefit the community in so many ways," said John C. Kerr, president of SFBR and chairman of TBAC.

Some cities have estimated that the economic impact of NBAF would be approximately $1.5 billion over 20 years. But Kerr said that NBAF's positive impact on San Antonio would not be limited to the economic benefits from the high-paying jobs, increased tax base and ripple effect through the area economy.

"Beyond that, we have spent 20 years now positioning bioscience as a leading industry for San Antonio," he said. "NBAF would be a validation of that effort. This would be seen nationally as putting San Antonio on the map as a major center for biomedical research."

While the healthcare and bioscience sector already is San Antonio's No. 1 economic generator, with an annual impact of more than $14 billion, Kerr compares the potential effect of NBAF landing in San Antonio to the effect that NASA had on Houston when it was located there in the 1960s.

Similarly, he sees the NBAF helping San Antonio to achieve the type of critical mass that helped Austin become established as one of the top centers for information technology, competitive with California's Silicon Valley. The more high-level research conducted in San Antonio, the more attractive the city becomes for bioscience companies, as well as top scientists, to locate here.



San Antonio has what DHS needs for the NBAF:

- **Research capabilities**
- **Workforce**
- **Acquisition/construction/operation** *(available land, infrastructure, utilities, relevant design and construction experience, affordability, high quality of life)*
- **Community support**

The impact on San Antonio's scientific research as well as commercial development of technology would be tremendous, he said, especially at the Texas Research Park, which was developed to enhance the city's potential as a leading research hub.

"Suddenly, you have a $500 million federal research center here," said Kerr. "It's hard to overestimate the impact of that."

What makes San Antonio an ideal NBAF site?

The NBAF will operate as a joint activity between the Departments of Homeland Security and Agriculture that will conduct research, development, and testing on specified infectious diseases in a state-of-the-art facility, including a biosafety level 4 (BSL-4) laboratory, the same type of maximum containment laboratory housed at SFBR's Department of Virology and Immunology. When SFBR's BSL-4 lab commenced operations in 2000, it was one of only three such labs operating in the United States and the only one not owned by the federal government.

Hence, San Antonio is the only location competing for the NBAF that has experience in the design, construction and operation of such a highly specialized research facility, and it has an impeccable safety record. In addition, the NBAF mission includes the development and testing of vaccines for infectious diseases affecting animals and humans, an area in which SFBR also has extensive experience, including the testing of vaccines in non-human primates.

Going into the competition, TBAC members believed that the San Antonio bid would get a boost from community support, one of the key criteria for DHS in its site selection process. The agency does not want to locate the facility in a place where it is not wanted.

"The support we have here for this type of research is unmatched," said Kerr. "None of the other sites has anything approximating the level of community support that we have here. It was typical of San Antonio to have this teamwork across the entire city, including the collaboration of two UT institutions, Brooks City-Base, the Texas Research and Technology Foundation, and SFBR in forming TBAC."

"We showed that, yes, there is community support in San Antonio for the NBAF and for the type of research it will conduct," said Dr. Jean Patterson, chair of SFBR's Virology and Immunology Department. "For

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the past eight years at SFBR, we've been working on the development and testing of diagnostics, treatments and vaccines for select agents such as Ebola, Lassa, Marburg and other viruses," she said. "We've done that safely and with enthusiastic support from the community. San Antonio is known as a city that is comfortable with high-level containment and that takes pride in local contributions to national security."

SFBR's experience with the type of pathogens of interest to researchers battling bioterrorism includes its participation in one of the National Institutes of Health's eight Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research. The Regional Center of Excellence that includes SFBR is a consortium of institutions led by the University of Texas Medical Branch at Galveston. The UT Health Science Center at San Antonio and UTSA also are members of this consortium, meaning these San Antonio institutions are already working together on projects related to NBAF.

Another key criterion for selection as the NBAF site is the existence of a broad research infrastructure in the community with relevance to the NBAF mission. TBAC demonstrated to the DHS site-selection team that San Antonio's existing research capabilities at institutions such as SFBR, UTHSCSA, Southwest Research Institute and UTSA are among the strongest of any of the original 18 sites under consideration. Among the city's many strengths, TBAC noted that the San Antonio has more than 110,000 people already working in healthcare and biosciences, including 4,500 jobs in bioscience research, 1,200 jobs in vaccine/pharma manufacturing, and 3,000 jobs in medical device and equipment manufacturing. Forty local scientists are acknowledged leaders in areas relevant to the NBAF mission, and the Alamo City also is now home to the largest military healthcare and biomedical research operations in the United States, providing unique collaborative and recruiting opportunities not available elsewhere. That will increase with the Defense Department moving functions here as part of the Base Realignment and Closure process.

York Duncan, president of the Texas Research and Technology Foundation, said the Texas Research Park site offers the best combination of requirements that DHS laid out for the NBAF: San Antonio's research capabilities, community acceptance, workforce, and infrastructure already exceed the capacity that the facility requires. "San Antonio offers the complete package," he said.

Where exactly would the NBAF go?

The 100-acre Texas Research Park site is adjacent to The University of Texas Institute for Biotechnology, part of the UTHSCSA's satellite campus there, housing its Department of Molecular Medicine, an important area of expertise for the NBAF.

Duncan pointed out that the site in western Bexar County has no endangered animals or plants, nor does it have any known historic or prehistoric sites, so he does not foresee any problems from the Environmental Impact Statement.

NBAF, he said, within five to 10 years would lead to a complete build-out of the 1,236-acre Texas Research Park, which has about 700 acres remaining for potential development.

"It will change that side of town," Duncan said. "It will bring a lot of new capabilities, veterinary, bioscience research, commercial development. Commercial and federal facilities are going to want to locate near the NBAF."

San Antonio could be 'just what the doctor ordered'

SFBR's Jean Patterson said another key factor in San Antonio's favor is quality of life. San Antonio is a place where highly educated scientists, many of them from major urban areas, would want to live, a key for the DHS' ability to recruit top scientific talent.

"What scientists are looking for is a scientific infrastructure where they can go to seminars and where they can interact with other scientists involved in molecular biology of pathogens and select agents, where they can talk about pathogenesis with other scientists," Dr. Patterson said.

In that regard, San Antonio offers the most advanced scientific community compared to the other, more rural sites under consideration. And as the nation's seventh-largest city, she said San Antonio would offer spouses of relocating scientists opportunities to find jobs comparable to those they are leaving.

"We have a robust scientific community, a city with a wonderful quality of life, a great depth of experience with this kind of work, and a community that is excited about San Antonio becoming a bigger player in the world of science," said Dr. Patterson. "What more could DHS ask for?"

Do cures already exist for Ebola, other threats?

SFBR is part of a national drug discovery and development program to identify approved drugs that could also be effective against biological weapons.

New research project aims to find out

Is it possible that a drug already on pharmacy shelves, or perhaps already sitting in your own medicine cabinet, could be used to treat infection with deadly pathogens such as Ebola, Marburg, and Lassa fever viruses?

That's something the federal government wants to find out as part of national biodefense efforts, and SFBR scientists have been asked to help answer the question.

The Foundation is part of a drug discovery and development program led by Silicon Valley-based SRI International to identify approved drugs that could also be effective against biological threats. The goal of the program – funded by the Defense Threat Reduction Agency of the Department of Defense – is to repurpose drugs that are currently FDA-approved and marketed but have not been previously evaluated against diseases caused by biological weapons.

"We're basically looking for a new indication for these approved drugs. So maybe on the bottle, instead of saying, 'For the treatment of breast cancer,' it might now say, 'For the treatment of breast cancer and Ebola infection,'" said Dr. Ricardo Carrion Jr., the principal investigator on the subcontract to SFBR.

Dr. Carrion said the odds of success are high. "Scientists have already repurposed drugs. For instance, there are some breast cancer drugs that are now being used to treat parasitic infections. Viagra is another example. It was originally developed to treat a heart condition, but now it's marketed for another purpose."

He believes that, with nearly 10,000 drug compounds that are known to clinical medicine, there is great potential that some of them could be effective against bio-threat agents such as Ebola, Lassa, Marburg, anthrax and tularemia. Some might even be effective against multiple agents.

"That's what the government wants," said Dr. Carrion. "They're looking for a magic bullet that could be used to treat multiple agents. That's important, because in the event of a biological attack, you wouldn't immediately know what agent had been released. It would be difficult for doctors to diagnose [patients], because infections with many of these agents initially cause the same symptoms. That's the case with Ebola, Lassa and Marburg. Doctors wouldn't necessarily be able to distinguish one from the other, or even from the flu, so if you have one drug that's effective against all of them, that's what you want to start treating patients with."

And the sooner drugs against biological agents are available, the better. That is a key reason for this drug-repurposing program. "It takes approximately 15 years and $1.2 billion to take a new drug from a chemical structure scribbled down in a notebook all the way to market," said Dr. Carrion. "In contrast, with drug repurposing, it's estimated to take just two or three years and $17 million to take a drug that's already approved into final FDA testing [for its new purpose] and get it out to market.

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> **This is a progressive move to try to protect the nation from the unthinkable."**
>
> **– Dr. Ricardo Carrion Jr.**

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"That means that this research has the potential to yield new defenses against biological attack at a fraction of the time and expense required to develop new drugs," he said. "Of course, then these drugs also would be available much more quickly for use in countries where these pathogens are endemic."

Some leading research institutions from across the country have teamed up to make this project happen. Leading the effort is SRI International, founded as Stanford Research Institute, which has a history of successful drug repurposing. Other institutes contributing research and technology expertise include SFBR, the United States Army Medical Research Institute of Infectious Diseases (USAMRIID), the University of Texas Medical Branch at Galveston, and BioRosettex.

Together, the institutes are working to develop a library of compounds, discover unknown activities against bio-threat agents, and confirm the effectiveness of the best candidates.

With BSL-4 capabilities and expertise in biodefense research with animal models, SFBR will soon be working to validate the leading "hits" found through screening by fellow collaborators.

Initially, collaborators will perform high throughput screening to identify drugs that show activity against the viruses. When the best candidates are identified, SFBR scientists will conduct animal studies to validate these drug compounds' effectiveness in a complete living system. A positive result there would put a drug on a speedy course to approval for use in the event of a biological attack.

"This is an exciting project, because it allows us to maximize the potential of drugs that are already on the market," said Dr. Carrion. "It's a progressive move to try to protect the nation from the unthinkable."

The Foundation's BSL-4 laboratory plays a vital role in this new biodefense project.

Study findings help explain why our sense of thirst declines with age

When it comes to staying properly hydrated, thirst may not be your best guide, especially if you're getting older.

That's because it is a well documented phenomenon that people's sense of thirst declines with age, which scientists say is a key reason for increased incidence of dehydration among the elderly. That, in turn, makes older adults more susceptible to other health complications, such as heat stress.

While this phenomenon has been well documented, its cause has not. Now, research findings by a team of scientists that includes Dr. Robert Shade of SFBR is shedding some light on the subject. In fact, in a December issue of the *Proceedings of the National Academy of Sciences of the United States of America*, the group revealed evidence showing that older adults get just as thirsty as younger adults, but their thirst is more easily satiated.

"We found that older adults get thirsty just as younger adults do, and when they get thirsty, they will drink, but [unlike younger adults] they don't drink enough to restore the water that they need to become 'normally hydrated,'" said Dr. Shade. "That's probably due to the fact that, as our study shows, the signal in a particular area of the brain that tells them to drink is 'turned off' with lower amounts of water."

The study – which includes collaborators from SFBR, the University of Texas Health Science Center at San Antonio, the Howard Florey Institute at the University of Melbourne, Australia, and the Baker Research Institute, also in Australia – was done with 12 healthy subjects in their 60s and 70s and 12 others in their 20s. All were given an IV infusion of a concentrated salt solution, which raises blood-sodium levels and stimulates thirst. Then participants were asked to rate their level of thirst and were given a PET scan, which produces images showing various aspects of brain function.

At that point, study participants were allowed to drink as much water as they desired, and when they were no longer thirsty, they were given another PET scan.

The results? Both the younger and older adults experienced the same intensity of thirst after infusion with the salt solution. The subsequent PET scan also revealed that in both groups the saline infusion activated an area of the brain called the anterior mid-singular cortex. That part of the brain "lit up" on the PET scan.

Afterwards, however, the older adults did not drink as much water in response to their thirst. Despite the fact that they still needed to consume more fluid to be properly hydrated, they no longer felt thirsty, and a PET scan revealed that the thirst signal in the brain had now been turned off.

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"So we found the area of the brain in which satiation of thirst is happening, and we found that smaller volumes of water are needed to deactivate the brain signal [for thirst] in older adults compared to younger adults. What we don't yet know is the reason why," Dr. Shade said. "We've speculated that there may be two possibilities."

He continued, "There is a fair amount of evidence in other areas of research which suggests that the amount of information being supplied from the body's peripheral receptors to the brain decreases with age. That may be what is happening in older people. It's possible that the signals that come from the periphery and contribute to thirst are lower in magnitude and more easily turned off. Our other speculation is that this particular area of the brain – the anterior mid-singular cortex – is more sensitive in older adults than it is in younger adults. But that is counterintuitive."

Dr. Shade said either hypothesis is just speculation until they can follow up this human study with more detailed investigations in mice. He said the research team's next aim is to see if these initial results can be replicated in mice and then to do functional studies that provide details on the physiological mechanisms that lead to these results.

"Once we have those details, it might be possible to devise a therapy or a drug to reverse the effect [and restore a proper sense of thirst in the elderly]," he said. "And the good thing is, now we know where to look to find those details. Before we did this study, we had no idea where the differences might lie between young and old when it comes to thirst."

Dr. Shade said the other good news is that people do not have to wait until the next phase of the study is completed to take action.

"Already, our study supports the notion that older people need to be aware that they should drink water on a regular basis and not rely on their thirst to tell them to consume fluids. I would caution that they should not drink too much, but instead be reasonable about it, simply making sure, out of regular habit, to drink adequate amounts of fluid on a daily basis."

What, exactly, is an adequate amount of fluid per day? "A good rule of thumb is six to eight 8-ounce glasses of water each day," said Dr. Shade.

This research is funded through a grant to the Florey Institute from the G. Harold and Leila Y. Mathers Charitable Foundation in New York.

Dr. Robert Shade prepares a research subject for a thirst test and PET scan.

Researchers learning how genes influence diabetes risk

Dr. Joanne Curran is examining 100 genes known to influence risk factors for diabetes.

SFBR scientists expect to make big leaps in their understanding of genetic influences on diabetes, thanks to a $1.7 million grant awarded to Dr. Joanne Curran, the grant's principal investigator.

The grant from the National Institute for Diabetes and Digestive and Kidney Diseases is allowing Dr. Curran and SFBR colleagues Dr. John Blangero and Dr. Jac Charlesworth to conduct a more detailed investigation on 100 genes that previous SFBR studies have shown to play a role in various risk factors for diabetes and other metabolic diseases. They are looking closely at DNA variations within the genes themselves to see how those changes affect the genes' output, and ultimately, how these genes exert their influence on such things as blood glucose and insulin levels and body fat.

"We're looking for functional changes within the DNA sequence of these particular genes that are causing certain individuals to have these risk factors for diabetes," Dr. Curran said. "Our previous work has uncovered genes that are influencing fasting glucose levels, body mass index, and other health traits related to diabetes risk. So now we want to find out how these genes vary among individuals and which DNA variations within the genes themselves impact their function and their resulting influence on human health.

"Then maybe we can find a way to target a particular gene and manipulate its function so that it doesn't result in high blood glucose levels, for example."

The need for new methods of preventing and treating diabetes is critical, as rates of type 2 diabetes, often called adult-onset diabetes, continue to climb in the United States and other first-world countries, particularly as obesity rates have reached epidemic levels. It disproportionately affects the growing Hispanic population, where the prevalence of type 2 diabetes is two to three times higher than in non-Hispanic whites. Obesity often precedes the onset of type 2 diabetes, which can make people more susceptible to a host of other health problems, including cardiovascular disease, kidney disease, and blindness. Type 2 diabetes accounts for more than 90 percent of diabetes worldwide, with scientists estimating that there will be 220 million cases worldwide by 2010.

"Right now, the best prevention we have for diabetes is lifestyle change," said Dr. Curran. "But what if you have a genetic predisposition that's causing your high levels of blood glucose? Then lifestyle changes alone may not help you. That's why we need to find the genes involved and the DNA variations that affect those genes' function. That will give pharmaceutical companies the information they need to develop new medications to fight this growing health problem."

The hunt for diabetes genes

SFBR geneticists have particular expertise in the search for genes that influence common complex diseases like diabetes and other disorders that are influenced by numerous

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environmental and genetic risk factors. In September of 2007, they announced a new research method they devised to speed up this cumbersome hunt.

That study, led by SFBR geneticist Dr. John Blangero, and detailed in the scientific journal *Nature Genetics*, utilized genetic material from blood samples from 1,240 participants in SFBR's ongoing San Antonio Family Heart Study. The San Antonio Family Heart Study includes approximately 1,400 members of 40 Mexican-American families in the San Antonio area, who are participating in a long-term investigation of the genetic determinants of heart disease, diabetes and obesity.

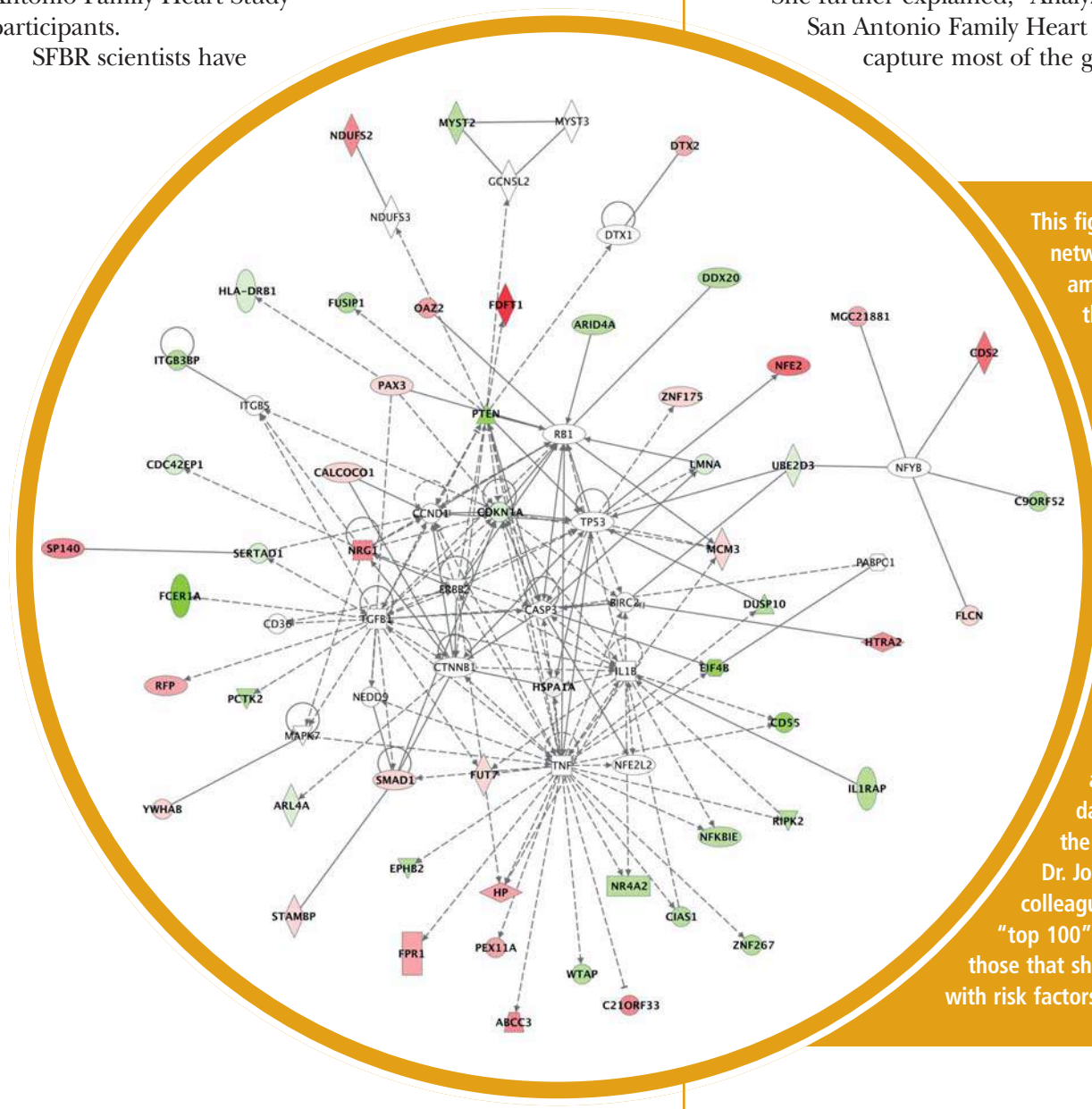
Instead of trying to sift through all 25,000 genes in the human genome, the researchers used transcriptional profiles – measures of the output of a person's genes – to identify genes that are self-regulated, or cis-regulated, meaning they harbor variations that affect their own output. That enabled them to rapidly narrow in on genes that likely have a causal effect on a particular disease or disease trait. In the *Nature Genetics* paper, the SFBR team described how it discovered the *VNN1* gene's influence on the level of HDL, or "good cholesterol," by statistically correlating the gene expression profiles with the variable HDL cholesterol levels in the San Antonio Family Heart Study participants.

SFBR scientists have used that same approach to find genes associated with other diseases, including 203 genes that correlate with risk factors for diabetes. From that list of 203 genes, Dr. Curran has selected the top 100 for further examination. She will look at the 100 genes that showed the strongest evidence of being self-regulated and the strongest correlations with diabetes risk factors such as a high level of glucose in the blood after a period of fasting, known as fasting glucose; other risks determined by tests of glucose and insulin; and a high level of fat as determined by assessment of the body mass index, the measure of fat in relation to height and weight.

What makes these genes tick?

In her more detailed investigation, Dr. Curran's group will utilize genetic samples from 182 founder individuals in the San Antonio Family Heart Study and search for variations in an area of the genes known as the promoter region, a key regulatory region of the gene. "By focusing on the promoter region, we're likely to find functional DNA variants within the genes, or variants that truly have a functional consequence in the cellular system, which is our ultimate aim," said Dr. Curran.

She further explained, "Analyzing the founders [of the San Antonio Family Heart Study] enables us to capture most of the genetic variation that's



This figure, referred to as a gene network, shows relationships among many of the 203 genes that a previous SFBR study found to correlate with diabetes risk. Each gene is represented as a shape, and the biological relationship between two shapes is represented as a line. Each shape is colored based on the diabetes risk factor correlation, and the intensity of the color indicates the strength (or significance) of the correlation (red is positive and green negative; the darker the color the stronger the correlation). In a new study, Dr. Joanne Curran and her colleagues will closely examine the "top 100" genes from this group, or those that show the strongest correlation with risk factors for diabetes.

present in the population without having to sequence everybody. These are the people who contribute most of the genetic information to the family trees in our study. So by picking those individuals, we really increase our chance of getting all the genetic information we need."

Impact on human health

Curran sees a two-fold benefit from identifying genes that influence our risk for diabetes. "Knowing you have a genetic predisposition for diabetes can be a wake-up call that you need to stay in shape and manage your diet to try and keep your blood sugar under control," she said. "But in cases where a person still exhibits those risk factors, despite lifestyle changes, perhaps a drug targeting genes that influence the risk factors can keep them under control."

The researchers also will test the findings of this study with two independent populations. One is in Wisconsin, the Metabolic Risk Complications of Obesity Genes Study, directed by Dr. Ahmed Kissebah, of the Medical College of Wisconsin, a co-investigator on Dr. Curran's study. The other is a group involved in the San Antonio Family Gall Bladder Study, directed by SFBR geneticist Dr. Ravindranath Duggirala, a consultant on Dr. Curran's study.

"By focusing on the promoter region, we're likely to find functional DNA variants within the genes, or variants that truly have a functional consequence in the cellular system, which is our ultimate aim,"
— Dr. Joanne Curran

Faculty Spotlight:

Dr. Thomas Folks boosts SFBR expertise in primate models, emerging viruses

This SFBR faculty spotlight introduces readers to Dr. Thomas Folks, the new associate director of research resources for the Southwest National Primate Research Center. Dr. Folks' impressive career includes 10 years with the National Institutes of Health and 19 years in leadership positions with the Centers for Disease Control and Prevention, where he was dedicated to the detection and identification of emerging viruses, as well as research and public health efforts to prevent the spread of HIV. Here he explains some of his accomplishments and how he is now using his expertise to advance the mission of SFBR and its primate center.

Dr. Tom Folks has joined the Southwest National Primate Research Center at SFBR after 10 years with the NIH and 19 years in leadership positions with the CDC.

Your background is so diverse: a master's degree from the Texas A&M University School of Veterinary Medicine with a thesis on a virus infecting horses; a Ph.D. from the University of Texas Health Science Center at San Antonio focused on leukemia; and postdoctoral fellowships with the Naval Medical Research Institute and the NIH focused on immunology. Then you served NIH as an expert in clinical immunology and assistant professor of pediatrics. That's before 20 years of work on HIV and other retroviruses. How did this interesting career path evolve?

My interest all along was immunology. For instance, my leukemia research was on the immunology of leukemia, examining white blood cell factors that modify immune response. My postdoctoral fellowships also were on human immunology, and that is where the twist came that led me into HIV research. I was one of the few people at the NIH in the early 1980s working with human white blood cells. This was the same time that AIDS broke out, and we didn't know the cause. One day, a lab chief brought in an unknown virus from France that a scientist there claimed to be the AIDS virus. He asked me to put this virus on the human cells in the lab, and it grew. That's the point where I could see a career develop before my eyes, and HIV became an integral part of my life.

Weren't you part of a major discovery about HIV while at the NIH?

Our group published the first paper showing that HIV can integrate into cells and lie dormant, then be driven out

of latency by various immune factors. That's when it starts replicating and causes disease. We showed this and demonstrated how latency works by developing cell lines that were latent, then putting certain immunological factors on these cells that activated the virus. As with all retroviruses, once HIV infects a cell, it jumps into the DNA of the cell and integrates itself into the genome. That's why you can't cure AIDS. Once you get infected, it becomes part of your body.

What were some of your greatest challenges and accomplishments at the CDC, where you served as the chief of the HIV and Retrovirology Branch, and later as the appointed chief of the Division of HIV/AIDS Prevention Laboratory Branch?

When I moved to the CDC, they wanted to develop a laboratory to prevent the next AIDS epidemic. What was needed before some other unknown virus jumped into humans and caused widespread disease was more surveillance and better epidemiology for emerging viruses. That became a very exciting part of my mission at the CDC. How do you find an unknown? We started devising sensitive generic assays (tests) that could be used to identify retroviruses that were jumping from nonhuman primates into humans, with the idea that we could screen risk groups – such as bush meat hunters or zoo workers – find an emerging virus and intervene before it created a new pandemic.

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It was when we began to take some of these new generic assays into the field that we discovered foamy virus emerging in the human population. All nonhuman primates can carry foamy virus, and they don't develop disease from it. Since the CDC first identified it in people, we've been monitoring 10 infected individuals in the U.S., and none of them have developed disease either. So it's probably safe in people, but we're not yet certain.

If foamy virus doesn't cause disease, is there any value in its discovery?

The question becomes: Can it be used as a tool for disease prevention or treatment? Would it make a good vector for gene therapy or for vaccines? That was the focus of my sabbatical at UCLA in 2000. I took the foamy virus, cloned it, and engineered it to express other genes, such as HIV and Ebola genes. Then I took the foamy virus expressing HIV genes and gave it to some primates, which resulted in an immune response to HIV.

Could that work lead to a successful AIDS vaccine?

Foamy virus would first have to be proven safe in humans over the long term. The concern with live viruses that integrate randomly into the genome is that they might disrupt a tumor-suppressor gene or turn on a tumor-enhancer gene. We don't see foamy virus doing that in primates or in infected humans followed retrospectively for 30 years. But we've only monitored a small number. With how many people and for what length of time do you need to study foamy virus before you're certain it's safe? That's a subject of debate.

My work at UCLA was proof of concept, showing that you can take a live, replicating, integrating vector, put disease genes into it, immunize an animal, and get a lifelong immune response. At this point, I wouldn't want to vaccinate a healthy child with foamy virus, but maybe you could use it as a vector for gene therapy in individuals with a terminal disease, perhaps using it to express insulin in patients with severe diabetes. If it cured their diabetes, you'd show its beneficial capabilities and, over time, accumulate the necessary data from a large enough set of people to show that it does no harm.

The CDC also is using it to create an Ebola vaccine for gorillas, which are in danger of extinction. What's ideal about using foamy virus to vaccinate animals in the wild is that it is a replicating vector. It can be transmitted from animal to animal. That means you could vaccinate a few gorillas, and they could "spread" the vaccine to many of the others.

Was foamy virus research your most exciting area of study at the CDC?

That was one, but my main mission at CDC was AIDS prevention. That included the development of nonhuman primate prevention models. Most people who study AIDS in nonhuman primates study how it causes disease. At CDC, we were asking, "How do we stop transmission?" Most of the

Dr. Tom Folks meets with SFBR geneticist Dr. Jeff Rogers, a core scientist with the primate center, about a proposed research project.

current preclinical models don't work effectively for transmission studies. Animals are given large amounts of the virus at one time, which is not the way HIV transmits naturally. So our goal was to develop a better model for transmission studies, and that is the low-dose repeat model, which mimics the way HIV is acquired in the human population. With this model, you can better determine whether it's possible to prevent HIV infection by intervening with vaccines, microbicides or drugs.

What prevention methods have you tested? Have any been successful?

We had the most success using AIDS drugs to prevent infection. We first showed that treatment with Tenovovir before exposure to the AIDS virus delayed infections two- to three-fold. If it took three exposures to infect the control group of untreated animals, it took nine exposures to infect the Tenovovir-treated animals. So if you were to give people this drug before exposure, you could make them three times more resistant to infection. We had even better results when we increased the potency of the regimen by coupling Tenovovir with a second antiviral, FTC. That treatment basically prevented 100 percent of infections. After 14 exposures, we could not infect the animals that had received the drug treatment. We published those findings this February in the online journal *PLoS Medicine.*

Is it a good idea for at-risk individuals to take these drugs for prevention?

Absolutely. Of course, there is some danger of behavior dis-inhibition. People might see this data, start taking the drug, continue their risky behavior, and then forget to continue taking the drug. But it is an effective prevention method if you keep up with it.

The coup de grâce *would be a vaccine. What is the progress on that front?*

We've come a long way with epidemiology, diagnostics, and AIDS drugs, but we're still a long way from a vaccine. The problem is that we've approached HIV as we have other viruses. Generally, vaccines that generate a good immune response protect people, but with HIV, it actually can enhance infection if you're pre-exposed and have an immune response. This is what the recent clinical trials have taught us. We still have a lot to learn about the immunology of HIV.

You hold 10 patents and three pending patents with colleagues from the NIH and CDC. What are the subjects of those patents?

Some are for cell lines that harbor HIV latently, which a number of commercial companies use to screen drugs. We also patented cell lines that produce HIV antigens,

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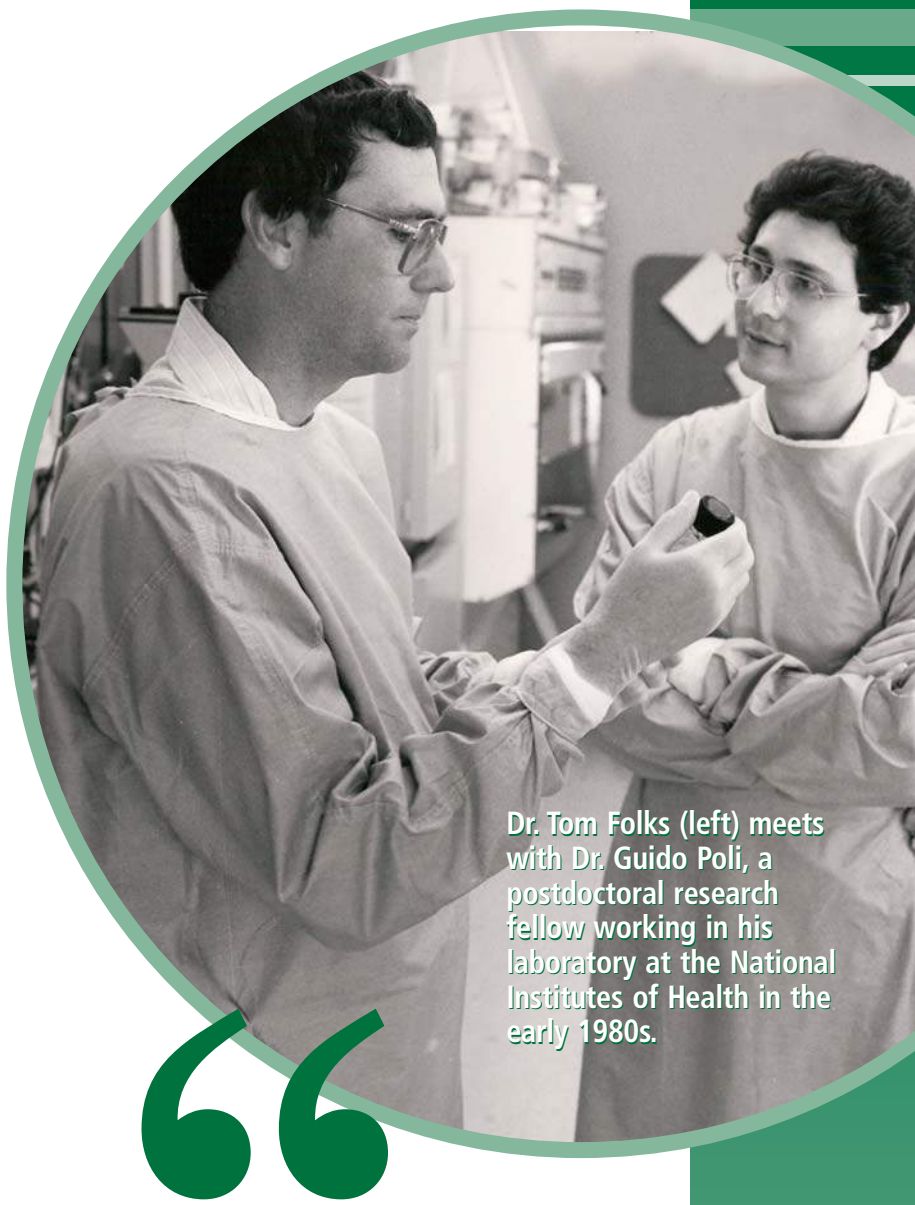

Dr. Tom Folks (left) meets with Dr. Guido Poli, a postdoctoral research fellow working in his laboratory at the National Institutes of Health in the early 1980s.

One day, a lab chief brought in an unknown virus from France that a scientist there claimed to be the AIDS virus. He asked me to put this virus on the human cells in the lab, and it grew. That's the point where I could see a career develop before my eyes, and HIV became an integral part of my life.

— Dr. Thomas Folks, associate director of research resources for the Southwest National Primate Research Center

Dr. Folks works closely with Dr. Bill Cummins, associate director of veterinary resources for the primate center, on the use of animal models in scientific research projects.

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which are not infectious. Companies use those when they don't want to work with HIV under containment. We also patented our generic assays for finding unknown retroviruses, and we patented two new human retroviruses that we found with those tests: human T-cell leukemia viruses 3 and 4. One of the most used of the recent patents is a generic retrovirus assay called AMP-RT, which can be used to identify any kind of retrovirus, animal or human. I've been speaking with people here at SFBR about incorporating this assay to screen our primates for unknown retroviruses. In that way, some of my work at the CDC might be used to help the scientists here.

Why did you leave CDC to join SFBR and its primate center?

After 19 years with the CDC, it's refreshing to apply my skills at a new place. I'm enthused about being here, because I would love to be able to help investigators in their pursuit of basic science. It's also like coming home. I grew up and did my schooling in Texas, and during graduate school in San Antonio, I used to come to SFBR. I collaborated with some of the scientists and learned a lot about primates from this center.

You mentioned supporting the scientists at SFBR. Would you talk more about your role here? What does an associate director of research resources do?

The coordination of a scientist's research project with nonhuman primates is a dynamic process. It involves such things as the Institutional Animal Care and Use Committee, which must approve every research program and protocol involving animals, funding, scheduling, the number of animals involved, the particular animals needed for the project, arranging space, and ultimately, getting everything established to carry out the concept design of the investigator. One of my primary tasks is to ensure that this whole process is smooth and streamlined. The system here already works admirably, but my job is to work with our team to smooth out any kinks. Another aim is to work with our focus groups – such as those focused on genomics, biodefense, infectious diseases, aging, etc. – to improve coordination and information sharing for greater synergy.

My external aim is to help as many national NIH grant recipients as possible have access to the primate center and to expedite their programs. Our primate center has 25 investigators from SFBR, but it has 155 affiliate collaborators from other institutions across the country. Expanding that external program and increasing our interaction with the other seven National Primate Research Centers is part of my mission here.

How might the various primate centers benefit from increased collaboration?

We want to develop a national consortium for different programs such as genomics, colony management, gene banking, and information technology to take advantage of unique expertise. We also want to set up electronic database access to resources and accomplishments so that researchers have improved access to the animals and the science that's being generated from them, to name just a few of our goals.

Have you brought any of your research programs from the CDC to SFBR?

That wasn't possible, but I hope eventually to bring some of my project ideas here and work with faculty to integrate them into SFBR research programs. We're well suited to utilize the low-dose repeat animal model for HIV transmission, for example, or to develop and test the foamy virus as a vector for vaccine delivery or gene therapy.

It's obvious that you're passionate about your work.

The most exciting thing for me is that I've been able to do this for my job. Every day I think, "Maybe God's going to show me something new today that he hasn't shown anybody else." That's pretty exciting, especially when you get to do it for a lifetime, and especially when you're fortunate enough to work with some truly great colleagues, as I have been. Great scientific advances are not generally made by a single individual, but rather, by cooperating groups working together to achieve a common goal. In my career, I've been blessed to work with such individuals and to be part of teams that helped spawn scientific discoveries. Now I'm happy to be part of the great research team at SFBR.

Trustee Spotlight:

J. Burleson Smith

J. Burleson Smith, known to friends as Burley, has played vital roles in the history and current success of SFBR, where he is trustee emeritus, and the law firm of Cox Smith Matthews Incorporated, of which he is a founding partner.

A regular Progress *feature is the "Trustee Spotlight," which highlights our stellar trustees and their contributions to SFBR and the larger community. For this issue, the editor was fortunate to speak with J. Burleson "Burley" Smith, whose involvement with the Foundation began soon after its inception. Upon his return to San Antonio after World War II, Mr. Smith began his legal practice with Seeligson, Cox & Patterson, predecessor to what is today San Antonio's top commercial law firm, Cox Smith Matthews Incorporated, of which he is a founding partner. His work on behalf of the firm drew him into involvement with the Slick family and the fledgling organization established by Tom Slick Jr., then known as the Foundation for Applied Research. Mr. Smith joined the board in 1946 and has offered his dedicated service ever since. We thank him for his commitment to SFBR and for his willingness to share his personal story with our readers.*

After law school, you joined the FBI as a special agent. Was that your career choice, or did you see U.S. involvement in World War II as inevitable, and the FBI was your preferred way to serve your country?

I graduated from the University of Texas Law School in 1940, and in 1941, I was in graduate school working on my master's degree in business. I had a considerable amount of work accomplished, but war clouds were gathering, and I knew I wouldn't have the chance to finish. So I applied to the FBI and to the Navy, promising myself that I would take a position with whichever one hired me first. It turned out that the FBI offered first – to my surprise and delight – so I accepted. Later on, I was stationed at the New York Field Office and was there at the time of the attack on Pearl Harbor.

That, unfortunately, was an exciting time in American and world history. Did your work as a special agent take you off on exciting missions?

I didn't do anything that a married man with children couldn't have done, but it was interesting work. I am grateful for my time with the FBI. Even its training school was

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interesting. One of the matters that was discussed there that I remember was the Urschel kidnapping case. I was not involved in the actual case, but it was the No. 1 case used as an example of what a helpful victim can do to solve a kidnapping. For us as agents, it showed us things we could do, questions we could ask to stimulate leads.

Are you referring to the highly publicized story of Charles Urschel's kidnapping from his Oklahoma City home by Machine Gun Kelly's gang in 1933?

That's right. Later on, when I returned to San Antonio and started work with the law firm, Mr. Urschel was one of our clients. By that time, he had married Berenice Slick, the widow of Tom Slick Sr., and the family had moved to San Antonio. While I was on a business trip with Mr. Urschel, he gave me the complete story of the kidnapping and following conviction. He told me how he paid close attention to a number of details, including the time of day that an airplane flew over their hideout, and how the FBI was able to use the information he provided to help lead to the gang's capture and conviction. It was particularly interesting hearing the story directly from the victim himself.

If your work with the FBI didn't take you off on adventures, your next area of service did. In 1943, you entered the Navy, where you were involved in combat.

I served as a night fighter director aboard a large aircraft carrier, the Ticonderoga, in the Pacific, and I had one really bad experience. We were about 75 miles off of Formosa when two kamikazes hit our carrier within 25 minutes. That didn't sink us, but it tore up the ship, disabled her, and caused many casualties. We had to be towed back to shore, and then the ship had to be rebuilt.

In 1945, after your discharge from the Navy, you came home and joined the law firm of Seeligson, Cox & Patterson. Were you there from the firm's inception?

No, I joined about four years after it was organized, soon after Oklahoma instituted a personal income tax and many of that state's fine business people started moving to Texas. I've heard John Cox tell the story of how that developed. One day Mr. Lamar Seeligson called him and asked, "What are you doing, John?'

John said, "I'm examining abstracts, just as any respectable lawyer does."

Lamar said, "Why don't you come over here and join Pat (L.M. Patterson) and me? We'll form a firm, and I'll catch the people from Oklahoma as they cross the Red River to avoid the state's personal income tax. The firm will represent them. I'll bring in the business, and you and Pat will do the work."

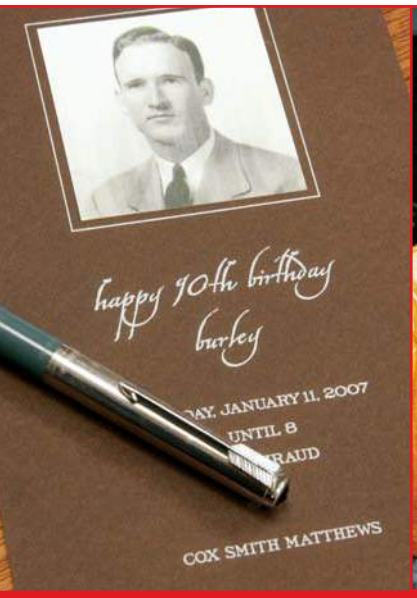
And that's how Seeligson, Cox & Patterson was formed.

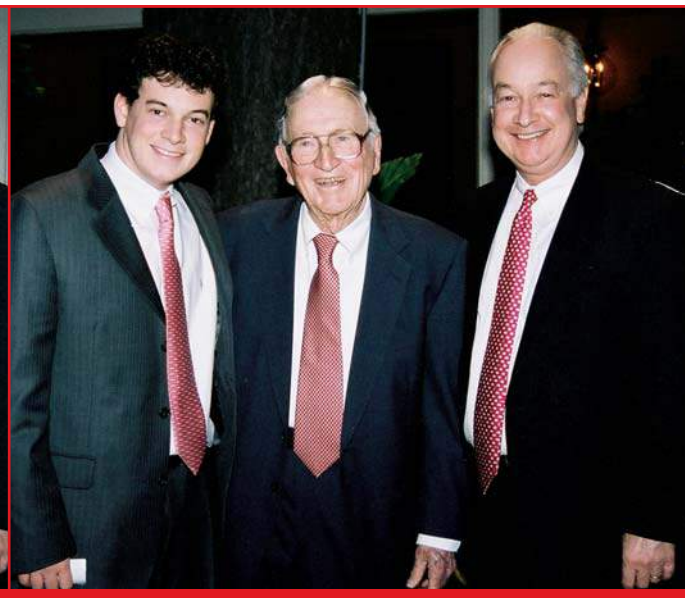
What kinds of work did you take on with the firm?

I started in oil and gas because that was about all the firm did in its early days. I became one of the lawyers for the National Bank of Commerce. Then, as we got bigger, we started taking on litigation. I was fortunate to represent some companies like Westinghouse and do anti-trust litigation. I also took on estate work. I'm grateful to have had a good, general practice with interesting work in a variety of areas.

As a young attorney, did you "cut your teeth" on legal work for the Slick family? They were one of the leading Oklahoma families to move to San Antonio.

Our firm certainly handled a great deal of the Slick family business, and I was involved in that representation. George Grant, who joined the firm around the same time as I, had





Scenes from Burley Smith's 90th birthday party include:

- **Burley enjoys some time with his children, Ellen, Terrell and Jamie.**
- **A reunion of the three men named "James Burleson Smith": grandson Burleson, Burley, and son Jamie**

been associated with the Slick family companies in Oklahoma. When the Slick interests moved to San Antonio, George moved with them and went into private practice with our firm. He handled much of their work until his retirement a few years later, and John Cox did as well. But Mr. Cox didn't want to travel, which guaranteed me a lot of work. The family's investments, and Tom's in particular, were so scattered. I did a great deal of traveling for Tom, mostly on matters involving oil companies in which he was interested. One case alone required me to make many trips across the country.

What was it like working with Tom Slick?

He was a delightful client to represent. He had confidence in people whom he chose for various functions, and he was thoughtful of everyone who surrounded him.

Tom knew more about more things than anybody I've ever known. He not only envisioned things; he stayed with them until they succeeded or it was determined that they weren't practical. People say he was a visionary, and that's true, but he was a visionary who didn't give up. And his vision pertained to so many interests, as is evidenced by Southwest Foundation for Biomedical Research, Southwest Research Institute, and the Mind Science Foundation. They're all different, but they wouldn't have been in existence without Tom, and they wouldn't have stayed in existence without Tom.

You handled the liquidation of Tom Slick's estate after he was killed in a plane crash in 1962. At the time, did you think his dreams would die with him or that a foundation had been laid that would allow them to carry on successfully?

Well, they did carry on, and much of that is attributable to his brother, Earl, and to his sister, Betty, and her husband, Lew Moorman. The family didn't let his interests die with

Retirement is not for Burley Smith, who still puts in a full week at the office.

him. They were great supporters. Lew was chairman of the Board of Trustees of the Foundation for many years, and Earl, even though he had already moved to North Carolina, remained enormously supportive.

You also have maintained a strong supportive role with the Foundation, serving as a trustee for nearly 62 years. Why have you been so committed?

I'm proud to have been associated with the Foundation, because I believe it's an outstanding contributor to the welfare of mankind. That sounds like a broad statement, but the

▶ *Continued on page 26*

Susan and John Kerr (center) visit with Burley Smith and his wife, Jane, at an SFBR reception. Burley's urging is part of what prompted the Kerrs to move from Houston to San Antonio.

- **A gathering of key members of Cox Smith: Dan Webster and Paul Smith, former managing directors; Jamie Smith, current managing director; and Burley Smith, former managing director.**

Trustee Spotlight, continued from page 25

medical research that the Foundation has supported through the years is truly extraordinary. I've enjoyed what the Foundation stands for, I've enjoyed the personnel, and I've enjoyed my involvement with the trustees, who form one of the strongest boards in San Antonio. It's drawn a lot of good people, with whom I'm honored to be affiliated.

One of those great SFBR trustees is your son, Jamie Smith, who also is a fellow shareholder with Cox Smith. Did he join the board because of his work with the firm or because he inherited your love for the Foundation's mission?

I like to think it was because of my interest in the Foundation, but he, too, is passionate about the Foundation's mission. I know he enjoys it, and I believe he's doing a very good job. I'm proud of his service to the Foundation, and I'm proud of his work with the law firm. After working as a briefing attorney at the Supreme Court of Texas, he moved to Houston and practiced with Vinson & Elkins, which is an outstanding firm. He was doing very well there, but under no pressure from me, resigned and accepted a position with our firm. He wanted to return to San Antonio, and we're thrilled to have him here. He's a fine attorney and a hard worker.

I understand that your influence also played a role in John Kerr's decision to move to San Antonio, which in turn led him to his active role with SFBR, first as trustee, then chairman, and now as interim president.

John is an outstanding lawyer and an outstanding person. He was practicing at Andrews & Kurth, which is a fine law firm in Houston, but I knew that his in-laws, Lew and Betty Moorman, and others in the family would love to see John and Susan back in San Antonio. Frankly, though, I wasn't thinking entirely of them. I wanted him here to join our firm. One day I called and asked him to consider moving, and from then on, it was a topic of conversation every time we saw each other. He finally did move to San Antonio, and he worked with us for a short time before moving on to other interests.

John has been a tremendous asset to the San Antonio community and to SFBR, stepping in at a difficult but very opportune time. His management abilities, his interest in the Foundation, and his good judgment have been a real boon to the Foundation.

"I'm proud to have been associated with the Foundation because I believe it's an outstanding contributor to the welfare of mankind."

– Burley Smith

At age 91, you're past retirement age, but you're not retired, are you?

Frankly, I'm proud of how our law firm has developed, and I'm grateful for the opportunities I've had and the wonderful people with whom I've had the privilege to work. I don't think about retirement because that would mean withdrawing from all of that. There is no question that I'm not as productive as I once was, but I like to keep in touch with the firm, particularly after our joinder with the Matthews group.

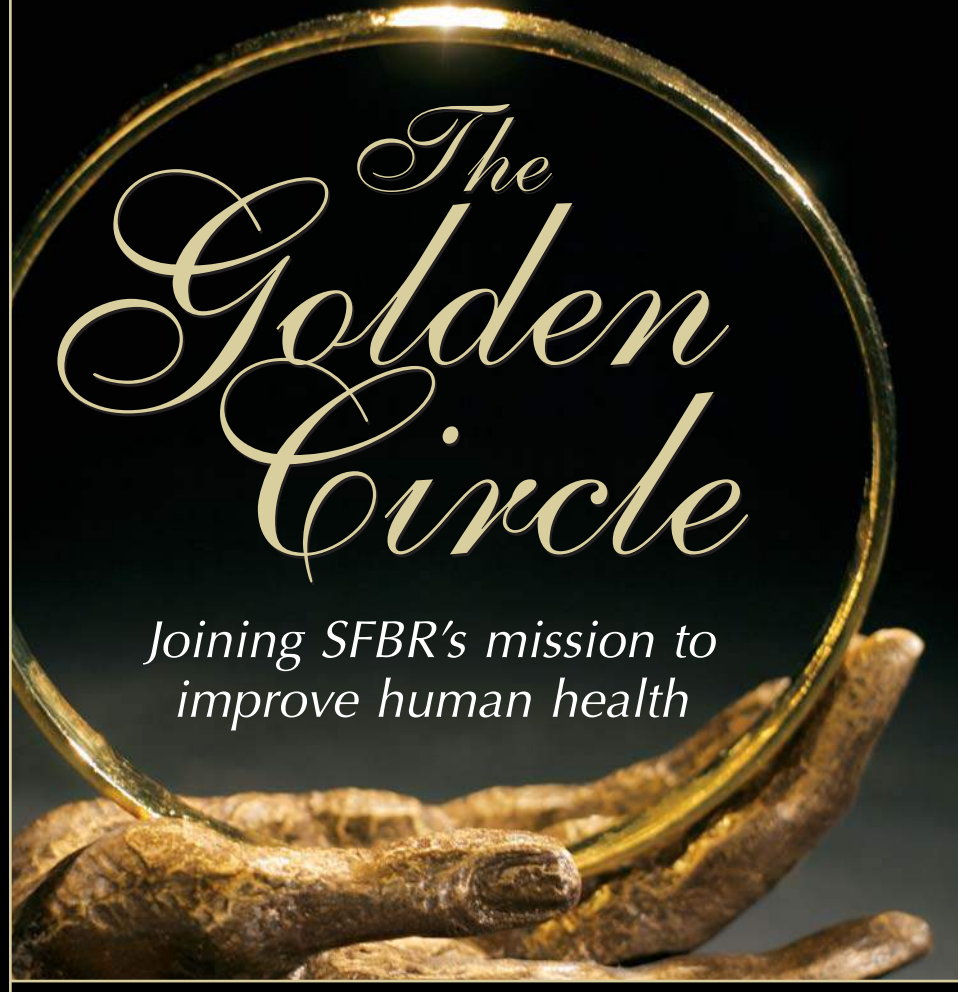
You also continue to hold some important civic positions: senior trustee of the University of Texas Law School Foundation; member of the Executive Committee of the Chancellor's Council of the University of Texas System; fellow of the Texas Bar Foundation; and trustee emeritus of the Southwestern Legal Foundation, to name a few. How do you keep up with it all?

I used to be very active with those groups and a number of others, including my church, Christ Episcopal. I believe I'm the oldest living ex-senior warden left at the church. I also enjoyed my six years on the Alamo Heights Independent School District Board. But anywhere that I'm still on the board, I'm in an emeritus position now.

After my first wife, Constance, died, I married Jane Carruth Flato, and we have been married for 28 years. We spend many weekends at Jane's lovely ranch in the Hill Country. I love going to the ranch, and I love spending time with my family and hers. That's where I get my greatest enjoyment.

Besides my son, Jamie, and his family here in San Antonio, my daughter Ellen and her family live in Virginia, and my daughter Terrell and her family live in Colorado. Jane's children are Ted Flato of Lake|Flato Architects and Malou Flato, the talented Austin artist. Today the children and grandchildren come see us more than we're able to travel and visit them. But they all love coming to Jane's ranch, and we all enjoy being together.

The Golden Circle



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

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

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

The Golden Circle

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

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

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

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

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

Please check the appropriate box:

- ☐ **Golden Circle,** unrestricted contributions of $1,000 or more to directly support indispensable biomedical research.
- ☐ **Benefactor Circle,** unrestricted contributions of $2,500 or more which also fund vital biomedical research.
- ☐ **President's Circle,** contributions of $5,000 or more to directly support the growing need for state-of-the-art equipment.
- ☐ **Chairman's Circle,** contributions of $10,000 or more to fund strategic initiatives that require immediate investment at the discretion of the Chairman and Board of Trustees.

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

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

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

_____
Spouse's Name

_____
Home Address ☐ ***Check if preferred mailing address***

_____
City State Zip

_____
Home Phone Business Phone

_____
E-mail

_____
Business Title

_____
Company or Foundation Name

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Business Address ☐ ***Check if preferred mailing address***

_____
City State Zip

Payment options:

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

☐ MasterCard ☐ Visa ☐ American Express ☐ Discover

_____
Card # Exp. Date

_____
Name on Card

_____
Billing Address

_____
City State Zip

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

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

Golden Moments

Golden Circle members are some of Southwest Foundation's most valued friends and supporters. A few of those individuals are shown here enjoying a recent event to thank them for their generosity and explain how their donations enable scientific progress.

Southwest Foundation Forum:

Expanding horizons in pursuit of better health

The ladies of the Southwest Foundation Forum just took us "Beyond the Sea" with their 2008 Gala on May 3, but throughout their 2007-2008 year, they've strived to take us beyond all expectations of what they can accomplish in support of SFBR.

As soon as the last decoration was put away from the record-setting 2007 Gala, which yielded $267,000 for SFBR pilot studies, the organizers of the 2008 Gala put the achievement in their rear view mirror and pushed full steam ahead in hopes of reaching an even higher goal this year.

While it will take a few months to determine this gala's financial payoff for biomedical research, there is no doubt the evening will be one to remember. But so, too, will other recent Forum events that have left their impact on members and on area high school students. The group sponsored two lecture luncheons for members, one in November and one in March. Both of these highly anticipated events sold out weeks in advance.

The Fall Lecture Luncheon featured Mary Kelly of the Austin office of the Environmental Defense Fund. She spoke on the topic of climate change and the need to be environmentally conscious, offering practical tips on how to be more eco-friendly.

The Spring Lecture Luncheon, titled, "Umbilical cords… What was trash is now treasure," spotlighted life-saving treatments that rely on umbilical cord stem cells, as well as the great potential for new treatments coming from this field of research.

The Spring Lecture Luncheon was also the occasion of the Science Education Awards, co-sponsored by the Forum and the V.H. McNutt Memorial Foundation to support innovative science programs at area high schools. With the goal of having a greater impact on a larger number of students, the Forum and the McNutt Foundation decided this year to increase both the amount and number of grant awards and to expand the geographic area from which schools can apply. In all, they awarded $20,000 in grants to six high schools from Bexar and contiguous counties: Medina Valley High School, first place, $7,000; Harlandale High School, second place, $4,500; Samuel Clemens High School, third place, $3,500; East Central High School, fourth place, $2,500; San Antonio Christian High School, fifth place, $1,500; and George W. Brackenridge High School, honorable mention, $1,000. In addition, the L.D. Ormsby Foundation made financial contributions to each school that applied for one of these awards.

Mother and daughter Barbara Dreeben and Lisa Sechler enjoy the Forum Evening Tour at SFBR.

SFBR President John Kerr visits with Forum board members Julie Dudley, Allison Zeller (2007-2008 president) and Jean Mitchell.

SFBR geneticist Dr. Laura Cox explains her research to Forum members and guests touring her laboratory.

The Forum also reached out to area high schools by organizing a series of student tours of SFBR between Jan. 15 and April 1. These tours are a tremendous learning opportunity for the high school students, who gain enthusiasm about the potential of science and the opportunities for careers in research.

Forum members and guests came to SFBR for their own tour on Oct. 24. Following a cocktail reception and welcome by SFBR President John C. Kerr, Forum members and other donors visited several SFBR laboratories and spoke with scientists about their ongoing research projects. It was one of those special evenings that allowed Southwest Foundation to thank the Forum for its support and Forum members to see firsthand the valuable research efforts they enable with their contributions of time, talent and treasure.

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

Founder's Council:

In the air there's a feeling of progress

Founder's Council 2008 President Sean McNelis, 2007 President Liesl Noble, and 2006 President Matthew Bell.

Dr. Melissa de la Garza accepts the Founder's Council's Steves Award from board members Brooke Peacock and Liesl Noble.

Spring is in the air, but in several SFBR laboratories, it's still mixed with the feeling of Christmas. That's because grants awarded to SFBR scientists at the Founder's Council 2007 Holiday Party have been used for the purchase of research equipment that impacts the scientists' work on a daily basis.

Totaling more than $27,000, the grant awards reflect the breadth of life-saving research underway at Southwest Foundation.

The council's premier award, named the Steves Grant in honor of the late Albert Steves IV, went to Dr. Melissa de la Garza, assistant veterinarian with the Southwest National Primate Research Center. She used the grant to purchase a NOMAD Portable X-ray Generator, an instrument that can take x-rays in the field. This instrument is highly beneficial to the care of SNPRC animal colonies, reducing the need to transport animals from their normal housing to the on-campus clinic when an x-ray is needed. That reduces stress on the animals and in turn positively impacts research done at the Primate Center.

Other grants were awarded to the following scientists:

- Dr. Jean Patterson, for a specialized computer that monitors and records data on experiments conducted in the BSL-4 laboratory;
- Dr. Krishna Murthy, for an instrument that determines cell growth and activation, used in research on AIDS, hepatitis, cancer and other autoimmune diseases;
- Dr. Jonathan Allan, for an instrument that concentrates HIV/SIV in plasma, utilized in AIDS research;
- Dr. Qiang Shi, for supplies that are required to investigate the use of bone marrow stem cells to treat heart attack victims;
- Dr. Tim Anderson, for a bench-top "shaker" used in his research on malaria.

The Tobin Estate served as the beautiful setting for this highly anticipated event, always a highlight of the Founder's Council year. Heartfelt thanks go to event sponsors – the Tobin Endowment and DPT Laboratories, Ltd. – as well as corporate sponsors of other Founder's Council events during 2007. Their generosity helped the Founder's Council maximize its grant awards, which are funded by annual membership dues.

The Founder's Council also used this special occasion to ring in the new year with a new slate of leaders. Liesl Noble, 2007 president, thanked outgoing Past President Matthew Bell for his years of service on the Founder's Council Board. She then stepped into the role of past president herself as she introduced Sean McNelis as president for 2008.

Other 2008 board members are Edward Hart, vice president membership; Craig Browning and Robert Finney, co-vice presidents hospitality; Brooke Peacock, secretary; John W. Feik Jr., treasurer; and members Michael Bacon, Chris Cheever, Dr. Ricardo Carrion Jr., Jack E. Guenther Jr., John R. Hurd Jr., and Jill Vassar.

The new year is off to an exciting start, with a unique evening of "Dining and Discourse" held at The Argyle on Feb. 25. After a cocktail reception and welcome by Founder's Council President Sean McNelis, guests joined one of 11 featured scientists or SFBR President John C. Kerr at the dinner table, where they enjoyed a dynamic dialogue focused on a particular research effort underway at SFBR.

This new event proved to be a popular one, generating lively discussion until late into the evening and earning enthusiastic reviews by Founder's Council members and SFBR scientists alike. Thanks go to three corporate sponsors whose generous contributions made the evening possible: Frost Bank; Goldman Sachs; and McNelis + Associates, PLLC.

Now the Founder's Council is planning a series of lecture luncheons featuring some of the Foundation's leading scientists, including Dr. Tim Anderson on May 14 and Dr. John Blangero on July 23.

For more information on upcoming events, or to join or renew your membership in the Founder's Council, contact Amy Abdalla at 210-258-9409 or amy@sfbr.org, or visit the council's Web site at http://www.sfbr.org/pages/founder_council.php.

Founder's Council members attending "Dining and Discourse" enjoyed lively conversations with some of SFBR's leading scientists, including (clockwise) Drs. Harald Göring, Sarah Williams-Blangero, and Andrew Hayhurst.

About Southwest Foundation

As one of the world's leading independent biomedical research institutions, the Southwest Foundation for Biomedical Research is advancing human health. Today, SFBR's multidisciplinary team of more than 85 doctoral-level scientists work together on approximately 200 major research projects.

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

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

Other extraordinary resources at SFBR include the nation's only privately owned BSL-4 laboratory, a critical asset to research related to biodefense and emerging infectious diseases, and the AT&T Genomics Computing Center, which houses the world's largest parallel computing cluster dedicated to human genetic research.

SFBR was created through the philanthropic vision of Thomas B. Slick Jr. in 1941, and it relies on philanthropy to sustain it today. Approximately 65 percent of its annual budget is funded from highly competitive, peer-reviewed federal research grants and contracts, while another 11 percent comes from commercial contracts with biotechnology and pharmaceutical firms. Philanthropy constitutes the second-largest portion of the Foundation's budget, as nearly a quarter of SFBR expenses are met by the generous contributions of foundations, corporations and individuals, as well as income and royalties from SFBR's endowment.

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

PROGRESS

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