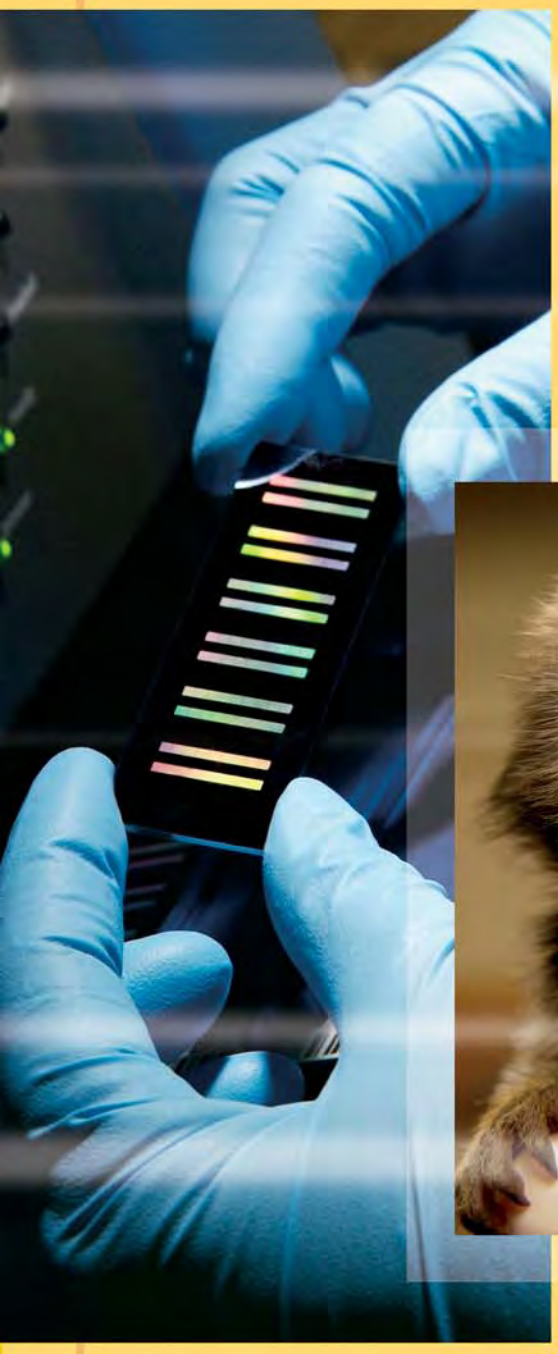
SFBR

Southwest Foundation for Biomedical Research

Report of Progress in 2006



About SFBR

As one of the world's leading independent biomedical research institutions, the Southwest Foundation for Biomedical Research is dedicated to advancing the health of our global community through innovative biomedical research. Today, SFBR's multidisciplinary team of 75 doctoral-level scientists work on more than 200 major research projects.

Located on a 332-acre campus in San Antonio, Texas, SFBR partners with hundreds of researchers and institutions around the world, targeting advances in the prevention and treatment of heart disease, diabetes, obesity, cancer, osteoporosis, 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, including a unique pedigreed baboon colony that is invaluable for genetic studies on complex diseases. The Foundation enjoys a distinguished history in the innovative, humane and appropriate use of nonhuman primates in biomedical research.

The Foundation also is home to other extraordinary resources that give its scientists and their collaborators an advantage in the search for discoveries to fight disease. With the nation's only privately owned biosafety level four (BSL-4) laboratory, designed for maximum containment, SFBR investigators can safely study deadly pathogens for which there currently are no treatments or vaccines.

Foundation scientists also have built the world's largest computing cluster for genetic and genomic research. Housed in the AT&T Genomics Computing Center, the parallel-processing network allows SFBR geneticists to search for disease-influencing genes at record speed.

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.

For more information on SFBR and its efforts to improve human health, contact the Foundation at 210-258-9400, or visit our Web site, www.sfbr.org.

Table of Contents SFBR

Credits

The SFBR Report of Progress in 2006 is a publication of Southwest Foundation for Biomedical Research.

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Letter from the President

During 2006, SFBR made a number of important strides in its pursuit of scientific excellence as one of the nation's leading independent biomedical research institutions. Despite a very difficult funding environment at the National Institutes of Health, our scientists achieved increases in both federal and non-federal research grants and contracts. We also continued to make solid gains in our commitment to build our permanent endowment and to put SFBR on the strongest possible financial footing. And, thanks to the generous support of our donors, we completed the latest phase of the major campus modernization program and capital campaign with the dedication of the 60,000-square-foot Earl F. Slick Center.

Independent research organizations like SFBR are highly dependent upon federal grants provided by the National Institutes of Health. Despite the fact that the NIH budget more than doubled between 1998 and 2005, it is substantially more difficult for researchers to obtain NIH grants today than it was in 1998. Writing in the journal *Science*, Elias Zerhouni, the director of the NIH, acknowledged this "paradox," which he attributed to a "doubling in the demand for grants . . . due to a large increase in the number of new scientists applying for grants."

This extremely tight funding environment has resulted in very difficult operating conditions for biomedical research institutions across the country. SFBR scientists nevertheless generated $33.1 million in federal grant revenue and $9.05 million in revenue from research contracts in 2006, increases of 7.3 percent and 11.3 percent, respectively, over 2005.

Compared with our peer independent research institutions, SFBR scientists rank among the highest in terms of grant awards per investigator, another benchmark of overall scientific excellence in the highly competitive world of federally supported basic research. Truly, our scientists' funding success speaks volumes about the high-quality, innovative nature of SFBR research and its potential payoff for human health.

We thank the many foundations, organizations and individuals who recognize the quality of our scientists' research and support it with their philanthropy. Research funding from donors continues to play an increasingly important role at SFBR, with new donor-sponsored research grants in 2006 totaling approximately $1.2 million. These philanthropic grants are especially critical to funding novel research projects when federal budgets are tight, and to helping SFBR scientists obtain the promising research data necessary to compete for larger federal grants in the future.

Another competitive edge for SFBR is the growth in its permanent endowment, which at the close of 2006 stood at $86.2 million, a 13.7 percent increase over the prior year and almost a tripling of the endowment since 1998. The importance of this strong endowment cannot be overstated for an independent research institute like SFBR – which does not have access to taxpayer support, tuition, or patient revenue – particularly in an adverse federal budget environment. The Foundation's total net assets at the end of 2006 stood at $141.7 million, with no debt on the balance sheet, a reflection of board policy to fund over $50 million in new and renovated buildings during the past decade with donor-contributed funds. In short, SFBR is in exceptionally strong financial condition thanks to the ingenuity of its scientists, strategic planning by the Board of Trustees, and the generosity of our donors.

In December of 2006, the Department of Genetics, the largest research department at SFBR, moved into its new state-of-the-art laboratories and offices in the recently dedicated Earl F. Slick Center, named in honor of the project's lead donor and the late brother of the Foundation's founder, Tom Slick. This marked the completion of the Foundation's ambitious campus modernization plan and accompanying capital campaign embarked on by the Board of Trustees in the late 1990s.

Although that plan is now complete, the modernization of the Foundation's laboratory and office facilities, particularly those relating to nonhuman primate research, is ongoing. I expect that later this year a new master plan for the campus will be presented for consideration by the board and that it will entail a number of major new building and renovation components. Just as technology continues to advance at a rapid pace, we must continue our quest to keep SFBR scientists in the state-of-the-art facilities necessary to stay at the forefront of leading-edge science.

Lastly, on a personal note, on June 28, 2007, I was succeeded by J.R. Hurd as chairman of the Board of Trustees. My nine years of service as chairman, which came during a period of major growth and development at the Foundation, was a deeply rewarding and gratifying experience. I was fortunate to work very closely with J.R. on all of our major board initiatives, and I know he will do a superb job in this leadership role.

The board has also requested that I continue in the position of interim president at least until mid-2008 as a national search for new leadership gets underway. I appreciate the confidence of the Board of Trustees, and I especially appreciate the dedication and support of SFBR's gifted scientists and administrators during this period of transition. It is an honor to work side by side with them in pursuit of our vital mission to improve human health through innovative biomedical research.

Respectfully submitted,

John C. Kerr

John C. Kerr
President

Board of Trustees

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Board of Trustees In Memoriam

Brig. Gen. Robert F. McDermott (USAF, Ret.)

July 31, 1920 – August 28, 2006

San Antonio and SFBR lost one of the city's most highly respected leaders on Aug. 28, 2006, when Brig. Gen. Robert F. McDermott (USAF, Ret.) passed away at the age of 86.

Accomplished in so many areas, "McD," as he was affectionately known, began his distinguished military career as a combat pilot in the European Theatre during World War II. After the war, he continued his military service first in Europe, then at the Pentagon, and after earning his master's degree from Harvard Business School in 1950, as an educator. He taught economics at West Point for four years before moving to the newly established Air Force Academy, where he was promoted in 1956 by President Eisenhower as the academy's first Permanent Dean of Faculty – as well as to the position of Brigadier General.

Following his retirement from the military in 1968, he moved to San Antonio and joined USAA as Executive Vice President. Within a year, he was at the helm as the organization's Chairman and Chief Executive Officer. Under 25 years of his guidance, the company reached new heights, as membership grew 400 percent; assets owned and managed jumped from $207 million to more than $30 billion; and the company was rated in 1993 as one of the country's best places to work. During his tenure, USAA also partnered with Opryland USA to start Fiesta Texas, now part of Six Flags, Inc.

Described by former San Antonio Mayor Lila Cockrell as "one of the absolute giants in terms of leadership in San Antonio" and by Gov. Rick Perry as "the face of economic development for years," Gen. McDermott did much during and after his time at USAA to improve San Antonio. He co-founded the San Antonio Economic Development Foundation and served as its first chairman from 1975-1980. Today, the organization is credited with bringing thousands of jobs and hundreds of millions of dollars worth of private investment to the city.

He also co-founded United San Antonio to promote social cohesiveness during the 1970s and 1980s, and, when Red McCombs put the San Antonio Spurs up for sale in the early 1990s, he assembled a team of local investors to buy the team and ensure its continued presence in the Alamo City. He also co-founded the Texas Research and Technology Foundation to attract bioscience and emerging technologies to the city, and he worked to gain state approval of graduate engineering programs at UTSA.

A member of the SFBR Board of Trustees since 1979, he has offered invaluable leadership to the organization. Both he and USAA have played a major role in support of the organization and have been key enablers of the Foundation's success. It is with a deep sense of gratitude that the faculty, staff and trustees of SFBR offer a final salute to this extraordinary gentleman.

Carlos Montemayor

November 21, 1945 – September 12, 2006

Carlos Montemayor, a legend in the Hispanic advertising industry who lent his expertise to SFBR as a member of the Executive Committee of the Board of Trustees, died at the young age of 60 on Sept. 12, 2006.

A San Antonio native, Mr. Montemayor started his career in Detroit, Mich., where he worked for an advertising agency specializing in the automotive industry. He returned to San Antonio to serve as the National Marketing Director for Church's Fried Chicken, then in 1983 founded his own advertising agency, *Montemayor y Asociados*, which soon became one of the largest Hispanic advertising agencies in the country, winning such clients as Chrysler, Pepsi, and Continental Airlines. In 2000, *Montemayor y Asociados* merged with GlobalHue, where Mr. Montemayor served as Vice Chairman until retiring in 2006.

Elected to the SFBR Board of Trustees in 1994 and to the board's Executive Committee in 2002, Mr. Montemayor supported the Foundation with his leadership, philanthropy, and skills in marketing and communications – skills that proved especially beneficial during his service on the Capital Campaign Committee from 2000 to 2005.

In addition to his service to SFBR, Mr. Montemayor was active in numerous areas of the San Antonio community, particularly with the Fiesta Commission, where he had stints as chairman and president. He also served on the boards of USAA Bank, Morningside Ministries, the Hispanic Chamber of Commerce, The Witte Museum and Our Lady of the Lake University. San Antonio surely misses this fine gentleman, described by city leaders as "a big man with an even bigger heart."

Earl Slick

November 20, 1920 – May 13, 2007

On May 13, 2007, SFBR lost one of the lifelong, guiding forces behind this institution's success, Earl F. Slick. Mr. Slick was present when his brother, Tom, founded Southwest Foundation in the 1940s and played a leading role on the Board of Trustees since its inception.

When Tom Slick died tragically in a plane crash in 1962, co-executors Earl Slick, Lewis J. Moorman Jr. and Charles Urschel stepped forward to help chart the course for the Foundation's future and keep it on a path to success. Mr. Slick's support – both personally and financially – continued throughout his life and is a major reason that SFBR today is one of the leading independent biomedical research institutions in the United States. Most recently, he served as the initial and lead donor to the Foundation's $40.3 million capital campaign to fund an ambitious campus modernization plan, including major renovations to the recently dedicated Earl Slick Center, which houses 60,000 square feet of genetics office and laboratory space and the Foundation's scientific library.

An aviator in World War II, Mr. Slick returned to San Antonio and founded Slick Airways, the first freight-only airline in the United States, pioneering a new industry that paved the way for Federal Express and United Parcel Service.

In the 1950s, he and his wife, Jane, moved to Winston-Salem, N.C., where he continued as a highly successful business entrepreneur in numerous areas ranging from real estate development to the lodging industry. He was one of the founders of Atlantic Aero, Inc., and he served on various community development commissions.

In addition, his philanthropy supported and advanced the visions of numerous organizations around the country, including educational institutions such as Wake Forest University and Phillips Exeter Academy; numerous historical institutions and museums; and the National Audubon Society.

SFBR extends a fond farewell full of heartfelt gratitude to a man who inspired us all in our pursuit of human progress through scientific research.

Irene Wischer

October 25, 1915 – March 23, 2007

On March 23, 2007, long-time SFBR Trustee Irene Wischer passed away at the age of 91. Mrs. Wischer, who also was active in politics and with many civic and community groups, is often described as a pioneer for paving the way for women in business, particularly in the oil and gas industry.

Mrs. Wischer started her career in the 1940s as an assistant corporate secretary for the Henderson Trust Company, an independent oil and gas company in San Antonio. By 1955, she had worked her way up to become a Director and Secretary/Treasurer of the organization. Then in 1963, she was elected President and CEO of Panhandle Producing Co., a diversified oil and gas pipeline company.

She was the first woman appointed to the executive committee of the Independent Petroleum Association of America, which she eventually chaired; a member of the National Petroleum Council; and a member of the Board of Directors of the Gas Research Institute. She also was the first woman to serve on the board of the Greater San Antonio Chamber of Commerce and the first woman inducted into the San Antonio Business Hall of Fame.

She also rose to numerous leadership positions in politics and public service. She served as State President of the Texas Federation of Republican Women; was appointed by President Ronald Reagan as Deputy Secretary of Energy; and was appointed by President Ford to the Citizens Advisory Council on the Status of Women.

Amidst all these commitments, Mrs. Wischer found a great deal of time and energy to work on behalf of numerous community and charitable groups, serving not only on the boards of SFBR and its sister organization, Southwest Research Institute, but also for such organizations as the San Antonio Medical Foundation, UTSA and the UT Health Science Center at San Antonio, the San Antonio/Air Force Community Council, the World Affairs Council, the Institute of Texan Cultures, KLRN Public Television, Alamo Heights United Methodist Church, and many other organizations.

Mrs. Wischer joined the SFBR Board of Trustees in 1980. Over the years, she was extremely generous to the Foundation, and most recently gave a significant gift to SFBR's capital campaign as an investment in SFBR's effort to recruit bright new scientists to its faculty. Her inspiring spirit and her dedicated commitment to the Foundation will be greatly missed.

Letter from the Chief Scientific Officer

Office of the CSO

2006 Doctoral Staff
(as of December)

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John L. VandeBerg, Ph.D.

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The year 2006 was another banner year for SFBR scientists, especially when viewed in light of two key areas that serve as measures of scientific excellence: the production of significant new research findings selected for publication in peer-reviewed scientific journals; and scientists' ability to garner major new research grants in a highly competitive funding environment.

The products generated by a biomedical research institution are publications in the scientific literature. Those papers report new knowledge about biological processes related to health and disease, thereby improving understanding of the mechanisms that convert healthy conditions to disease states. Reports of research results and interpretations of their bearing on human health and disease provide the critical foundation of knowledge upon which other scientists, primarily in the commercial sector, build and translate basic science into new drugs, vaccines, and medical procedures that will ultimately improve the health of our global community.

In 2006, SFBR scientists were authors on 131 articles in the international scientific literature. Each article is the result of years of painstaking research and a rigorous selection process carried out by the editors of the journals and the peer reviewers from whom they receive critiques. The key research findings documented in these publications are highlighted in the following reports of the SFBR research departments and the Southwest National Primate Research Center. I encourage you to read through this annual report and see the strides our scientists are making in their effort to defeat such maladies as cardiovascular disease, diabetes, cancer, diseases of aging and of premature birth, psychiatric disorders, and infectious diseases such as HIV/AIDS, hepatitis C, dengue, malaria, tuberculosis, and countless others.

Despite the diminution in funding available from the National Institutes of Health to support basic biomedical research, SFBR scientists were highly successful during 2006 in generating new grants and contracts. Nine grants from NIH and one from a contract commercial source were for $1.5 million or more in support. The new grants and contracts received in 2006 totaled $31.7 million, up from $30.6 million the previous year. This 3.6 percent increase in new awards is testimony to the capabilities of our scientists to outperform their peers at a time of increased competition for fewer available research dollars. These new grants and contracts will influence the directions of our research in the years ahead.

Five of the major NIH grants were awarded to support research on the genetics of susceptibility to complex diseases in humans. Dr. Jean MacCluer was awarded a $4.1 million grant to support the continuation of the Strong Heart Family Study, a long-term study of the genetic determinants of heart disease in Native Americans, for an additional four years. Dr. John Blangero received a $3.6 million grant to explore the roles of genes in determining normal variation in brain structure and function. The results of this research will have major implications for our understanding of psychiatric disease and other brain-related disorders. A five-year, $2.3 million grant was awarded to Dr. Eric Moses to support his search for genes influencing susceptibility to preeclampsia, the most common major disorder of human pregnancy. Dr. Harald Göring received a four-year grant totaling $1.9 million in funding to investigate the effects of genes that influence susceptibility to common infectious agents that contribute to heart disease. All of these major genetic studies rely on the use of innovative statistical tools for the analysis of genetic data that were developed at SFBR by Dr. John Blangero and his associates That work also got a boost in 2006, with a five-year, $3.9 million grant awarded to Dr. Blangero for continued support of

the development of novel analytical tools and software for genetic research.

Another area that will be supported by major new NIH grants is research on infectious diseases. Dr. Tim Anderson received $2.3 million for five years of support of his efforts to identify genes that control drug resistance in the mosquito-borne parasite that causes malaria. A four-year, $1.7 million grant was awarded to Dr. Rebeca Rico-Hesse to support her work on the determinants of virulence and transmissibility of viruses that cause dengue fever.

Primate research is a third focus area that received a major influx of funding in 2006. Dr. Bill Cummins received a $2 million contract from a commercial company to continue the management of a breeding colony of more than 1,000 cynomolgus monkeys that are being used to test the safety and efficacy of drugs. Dr. Luis Giavedoni received a $1.7 million, four-year NIH grant to establish new technologies for assessing immunological responses of monkeys to vaccines.

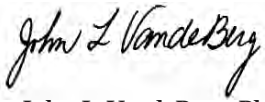
The 10th of the new grants totaling $1.5 million or more was an NIH grant of $1.5 million to Dr. Susan Mooberry to support her investigation of the mechanisms by which new anti-cancer drugs exert their chemotherapeutic effects.

Another significant accomplishment during 2006 was the strengthening of our cadre of principal investigators with the appointment of four additional scientists to the rank of assistant scientist. Dr. Marie-Claire Gauduin joined the Department of Virology and Immunology from Harvard Medical School. Her addition to the faculty significantly strengthens our research programs using the rhesus monkey model to improve technologies for the prevention and treatment of AIDS. Dr. Ricardo Carrion Jr., formerly a staff scientist in the Department of Virology and Immunology, also was appointed to the faculty in 2006, strengthening our capabilities in high biocontainment research. The Department of Genetics gained two new faculty members with the appointments of Drs. Joanne Curran and Lorena Havill. Dr. Curran brings specialized expertise in molecular genetics to the department, and Dr. Havill has expanded the department's complex disease focus to include research on the genetic determinants of bone metabolism and osteoporosis.

We also appointed two new veterinarians to the faculty of the Southwest National Primate Research Center. Dr. Patrice Frost joined us as an associate veterinarian and is now responsible for the oversight of the center's macaque colonies. She had previously worked at the New Iberia Primate Research Center. Dr. Melissa de la Garza had been a staff scientist at the SNPRC and was appointed to the faculty as an assistant veterinarian. She is responsible for managing the Animal Biosafety Level 3 facility, which is critical for our infectious disease research programs utilizing nonhuman primates, including an exciting new program funded by NIH in 2005 and aimed at developing a vaccine for tuberculosis.

In July of 2006, I was appointed to the position of chief scientific officer at SFBR, while continuing in my capacity as director of the SNPRC. I am honored to lead the SFBR scientific enterprise in this capacity, and I look forward to working with all of the SFBR stakeholders during the exciting and productive years that lie ahead for the Southwest Foundation for Biomedical Research.

Sincerely,



John L. VandeBerg, Ph.D.
Chief Scientific Officer

Department of Genetics

The Department of Genetics continued to advance as a world leader in genetic studies of complex diseases during 2006. The exciting upward trajectory of the department's established research programs led to new discoveries and significant methodological advances that were chronicled in more than 80 articles published by SFBR geneticists in the scientific literature. Eighteen of those articles reported new gene localizations, or chromosomal locations known to contain a gene influencing a particular disorder. In addition, scientists leading the department's newest research initiatives generated major funding to support the expansion of ongoing research programs into new areas. The department's scientific and funding achievements in 2006 will facilitate even greater progress in 2007.

Since its founding in 1982, the Department of Genetics has focused on addressing the most important public health problems facing the United States through the use of genetic techniques to identify new mechanisms for the diagnosis, prevention, and treatment of illnesses. During the last 24 years, the Department of Genetics has developed unique expertises, resources, and research tools to better enable it to address the department's mission of advancing human health through basic biomedical research with animal and human populations. Departmental scientists have reconstructed and characterized many of the largest human pedigrees available for genetic research and have created unique pedigreed colonies of animals for use in research. They also have pioneered the development of statistical and genetic tools for gene discovery. During 2006, the department's cutting-edge research programs yielded new insights about many critical public health concerns, including heart disease, diabetes, insulin resistance, gallbladder disease, obesity, preeclampsia, osteoporosis, and psychiatric disease.

Identifying the genes that influence the world's leading public health problems

Heart disease. Heart disease is the leading cause of death in the United States, killing over 700,000 people each year. The American Heart Association has estimated the yearly costs of health care and lost productivity associated with heart disease at over $250 billion. Historically, the Department of Genetics has focused the majority of its efforts on localizing and identifying genes that determine susceptibility to heart disease in order to identify new biological pathways that can be targeted in the development of more efficacious treatments and preventions for this disease.

Strengthening ongoing research on cardiovascular disease in American Indians, Dr. Jean MacCluer received a major grant totaling $4.1 million to provide five additional years of support for the Strong Heart Study. This program is assessing the genetic determinants of heart disease in 3,600 American Indians from Arizona, Oklahoma, and the Dakotas. Working with this research group, Dr. MacCluer hopes to identify genetic factors that put American Indians and other minority populations at disproportionately high risk for heart disease, as well as genes that influence disease susceptibility in the broader population.

Although researchers have explored the impact of many environmental factors on disease risk, the role of common infections in the development of heart disease has been little studied to date. In 2006, Dr. Harald Göring initiated a revolutionary study that is aimed at assessing the link between genetic susceptibility to common infections such as herpes simplex virus 1 (the cause of cold sores) and *Helicobacter pylori* (a major cause of ulcers) and risk for development of cardiovascular disease.

A number of epidemiological studies have shown a higher-than-average prevalence of these and several other common chronic infections in people who have suffered heart attacks, strokes, and a variety of other ailments. A leading hypothesis explaining this correlation is that chronic infections lead to a chronic state of inflammation as the immune system works continuously to fight off the infection. Inflammation is a known risk factor for heart disease and many other disorders associated with

aging. So, in a study that is a first of its kind, Dr. Göring is searching for genes that influence a person's susceptibility to seven of these common chronic infections and then exploring their link to heart disease risk. He believes the study's findings could help scientists find better ways to control infections and ultimately reduce risk for cardiovascular disease and other conditions affected by inflammation. This work is supported by a major new grant totaling $1.9 million awarded in 2006 by the National Heart, Lung, and Blood Institute.

Diabetes. Type 2 diabetes is a burgeoning public health problem that is rapidly reaching epidemic proportions in the United States, with about 20 million people affected. Dr. Ravi Duggirala has conducted extensive research on the influence of genetic factors on metabolic syndrome – a precursor to heart disease and diabetes – and risk factors for type 2 diabetes in Mexican Americans. During 2006, his research program produced two major findings published in the scientific literature. First, Dr. Duggirala and his colleagues localized a gene that influences birthweight to a region on chromosome 6. Birthweight affects health throughout a person's lifespan and is a known risk factor for adult onset diabetes, so the discovery of this gene and how it works could potentially provide new targets for the prevention and treatment of diabetes and other health problems. In another significant paper, Drs. Duggirala and Sobha Puppala reported the results of the first genomic search for genes influencing gallbladder disease, a painful digestive disorder related to diabetes, which determined that a gene on chromosome 1 influences differential susceptibility to the disease.

Pregnancy disorders. Preeclampsia, the most common major disorder of human pregnancy, is associated with severe hypertension in the mother and preterm birth of the infant. The disease results in over 70,000 maternal deaths throughout the world each year and is a leading cause of pre-term delivery, which can have ramifications on the health of the infant for a lifetime. Little is known about what causes preeclampsia, leaving doctors with few options in treatment of the disorder, but it is evident that genetic factors play an important role. Therefore, the discovery of genes that influence susceptibility to preeclampsia would facilitate the development of predictive diagnostic tests that will improve management of the disease, and it could lead to the development of new treatments.

In a major advance for understanding the determinants of preeclampsia, Dr. Eric Moses published a paper localizing a gene influencing this disorder to a region on chromosome 2. This exciting research will now be expanded under support from

the National Institute for Child Health and Development, which awarded Dr. Moses a grant totaling $2.3 million in 2006.

Psychiatric illness. Another major area of public health concern is psychiatric illness. Departmental scientists have been active in research on the genetic determinants of psychiatric diseases, including depression, schizophrenia and alcoholism. An exciting new addition to this research area is Dr. John Blangero's project on the genetic determinants of normal brain structure and function, which is supported by the National Institute of Mental Health through a $3.6 million grant awarded to SFBR in 2006. This cooperative project, which is being done in collaboration with Dr. David Glahn and his colleagues at the University of Texas Health Science Center at San Antonio, involves cognitive testing and MRI brain scans of 1,000 Mexican Americans who previously participated in the San Antonio Family Heart Study. In the largest study of its kind, researchers are trying to learn more about normal brain structure and function – and the genes involved – in order to shed light on what goes awry in people with mental illness and brain-associated disorders such as Alzheimer's and Parkinson's disease. The potential pay-off could be the discovery of new venues for treating the root causes, rather than merely the symptoms, of these devastating disorders.

Parasitic diseases. In addition to research programs on diseases that dramatically impact the health of the U.S. population, the Genetics Department also has major research efforts focused on the parasitic diseases that are the primary public health burdens in the developing world. Dr. Tim Anderson has focused his research on malaria, which is a leading global health problem that results in over a million deaths per year. Between 350 million and 500 million people contract malaria each year, and one of the major barriers to effective control of the disease is the emergence of drug resistance in the parasitic organisms that cause malaria. This year, Dr. Anderson received a large grant award totaling $2.3 million from the National Institute of Allergy and Infectious Disease to continue his research on genes influencing drug resistance in malaria parasites. This research promises to improve our understanding of the causes of drug resistance and to facilitate the redesign of drugs to improve their efficacy in combating malaria.

Creating innovative resources and tools for gene discovery

Animal models allow scientists to address research questions that cannot be addressed in human studies, because it is possible for researchers to control both environmental and genetic factors when conducting animal research. Here again, SFBR's Department of Genetics is a world leader, with a long history of developing unique animal models for genetic research on major public health problems.

The laboratory opossum model for biomedical research. For example, the South American opossum *Monodelphis domestica* was developed as a laboratory animal by Dr. John VandeBerg and has been widely used as a model for research on skin cancer, cardiovascular disease, neonatal development, and the repair of spinal cord injury. In 2006, Dr. VandeBerg received a generous grant from the Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation for the continued maintenance and research use of the Southwest Foundation's *Monodelphis* colony. In addition to being a source of animals for collaborative research programs throughout the world, the colony is critical to ongoing genetic research by departmental scientists. In 2006, Dr. Nico Gouin's research resulted in a key paper that localized the major histocompatibility complex region, an area of genes important for immune function, in *Monodelphis*. This work will significantly enhance the value of the laboratory marsupial for research on inflammation and immunity.

Mapping the baboon and rhesus genomes. To identify specific chromosomal regions that contain genes affecting particular traits or disease susceptibilities, scientists require a map of locations of genetic markers – or identified places along the genome where genes vary from one person or animal to another. While the human genome project provided scientists with this tool for studies of humans, gene maps are not available for many animal models used in research. Departmental scientists pioneered the development of gene maps for nonhuman primates when Dr. Jeff Rogers and his colleagues developed a gene map for baboons several years ago. This baboon gene map has facilitated rapid advances in the detection of genes influencing a broad range of common disease processes in the baboon model. In a major scientific advance in 2006, Drs. Laura Cox, Michael Mahaney, John VandeBerg, and Jeff Rogers published the second-generation genetic linkage map for the baboon genome, providing scientists with a significantly improved gene map to use in localizing and identifying genes.

While the baboon has been the model of choice at SFBR because of its suitability for cardiovascular disease research, the rhesus macaque is by far the most widely used primate model in biomedical research. Around the country, it is the primary model for investigations on AIDS, neuroscience, addiction research, vision research, diabetes and pharmacology. However, the utility of rhesus monkeys for assessing the genetic determinants of disease has been limited by the lack of a gene map for this species. Over the past several years, Dr. Jeff Rogers has directed a major effort to develop a gene map for this critical species. This effort resulted in the publication in 2006 of the first genetic linkage map for the rhesus macaque genome. The availability of a rhesus gene map will significantly expand the range of research that can be conducted with rhesus monkeys.

Statistical methods for genetic and genomic research. Development and testing of statistical methods for genetic studies has been a major research focus within the Department of Genetics since its inception. Dr. John Blangero is an internationally recognized leader in the development of new statistical techniques for the detection of genetic effects on complex traits such as blood cholesterol, hypertension, glucose levels and other physiologic conditions influenced by multiple genes and environmental factors. The novel methods developed by Dr. Blangero and his SFBR colleagues for gene localization have been implemented in the computer program SOLAR, which now has over 3,000 registered users around the globe, making it one of the

world's most widely used tools for statistical genetic analysis. SOLAR has been used for the majority of gene localizations for quantitative traits reported in the scientific literature over the last five years. In 2006, Dr. Blangero received funding to support an additional five years of research on developing new computer-based techniques for gene mapping in large human pedigrees as part of his NIH MERIT award – a prestigious award bestowed on less than 1 percent of NIH-funded researchers during their scientific careers. This grant, totaling $3 million, will support the development and expansion of statistical genetic techniques included in the computer program SOLAR.

Applying cutting-edge technologies to novel problems

While the novel analytical methods developed in the Department of Genetics have been focused on common diseases, departmental scientists now are using them as part of an innovative study of a rare monogenic disorder, cystinosis. This devastating disease appears in early childhood and is associated with the accumulation of cystine in cells, which results in damage to the kidneys and eyes. During 2006, the Azar family continued to support a research project directed by Drs. John Blangero and Eric Moses that is designed to uncover the biological pathways involved in cystinosis. The project has not only yielded new insights into the genetic control of cystinosis but also has generated information on large-scale gene expression that is revolutionizing approaches to the investigation of common complex diseases.

Working in state-of-the-art facilities

In addition to making significant scientific progress during 2006, the Department of Genetics moved into new space in the Earl Slick Center at the end of the year. The 60,000 square feet of space in this research complex received major renovations with donor funding from the Foundation's recent capital campaign. The new state-of-the-art laboratories, office spaces, and equipment in the Earl Slick Center provide unparalleled opportunities for genetic research. Together, the outstanding resources of the Earl Slick Center and the AT&T Genomics Computing Center – which houses the world's largest computing cluster for statistical genetics – give the Department of Genetics a unique edge in the competitive world of science that will allow it to rapidly accelerate the rate of progress in 2007 and beyond.

2006 Doctoral Staff

(as of December)

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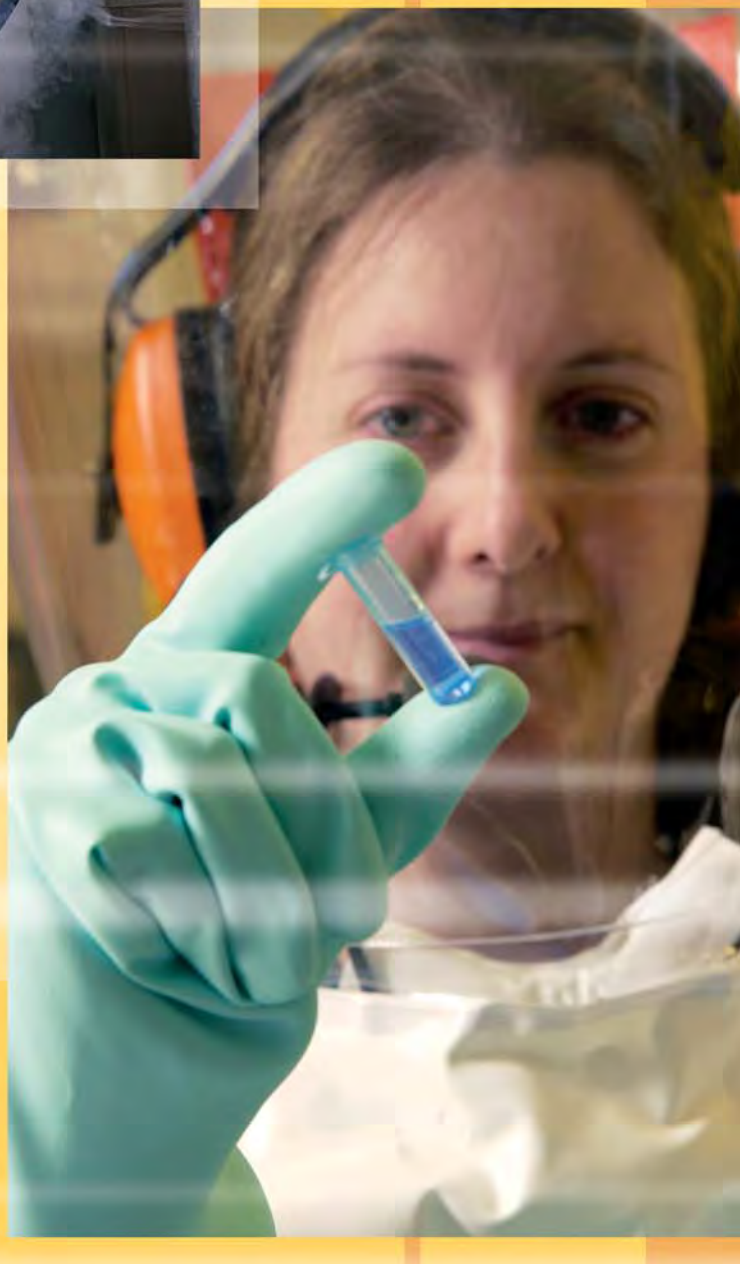
Amanda Vinson, Ph.D.
Venkata Saroja Voruganti, Ph.D.
Deidre A. Winnier, Ph.D.

Department of Virology & Immunology



To defeat viruses that cause AIDS, hepatitis, herpes, hemorrhagic fevers and a host of other devastating diseases, scientists in the Department of Virology and Immunology are studying how these viruses replicate and propagate, how the human immune system recognizes them, and how to stimulate the immune system to clear viral infections.

To assist in these efforts, SFBR virologists have access to some of the best-equipped laboratories in the world, including the nation's only privately owned biosafety level four (BSL-4) maximum containment laboratory. Also extremely valuable to their research efforts is SFBR's Southwest National Primate Research Center. Animals at the center offer the most effective models for human infectious disease, as well as for the evaluation of therapeutic drugs and vaccines against viral agents.

Fending off bioterror and emerging infectious diseases

Animal model development and preclinical vaccine studies. In the effort to protect the nation from the threat of potential bioterror agents and emerging viruses, SFBR virologists apply their skills toward developing and testing novel detection methods, diagnostics, vaccines and therapeutics for these deadly pathogens, as well as toward the development of animal research models that make this testing possible. While research with animals is important to investigations on most areas of human health, it is especially critical to biodefense efforts.

Because natural infection with many of these agents is uncommon, and because in many cases there are no effective treatments or vaccines, it can be unethical to conduct human trials. That is why the Food and Drug Administration enacted its "two animal rule" stating that new vaccines and therapies for many of these agents can be approved for use in humans if they prove safe and effective in two animal models. For this reason, SFBR scientists have dedicated themselves to finding animal models in which infection closely mimics what occurs in humans who contract these diseases.

On this front, SFBR virologists had a great deal of success in 2006. Dr. Jean Patterson and her research team demonstrated the first use of the common marmoset monkey in efficacy testing of a vaccine against Lassa hemorrhagic fever. The group first showed the validity of this animal model for Lassa infection in 2005, and in 2006, tests with marmosets showed that an ML29 live attenuated Lassa fever vaccine was 100 percent effective in protecting these small nonhuman primates against lethal challenge with the virus. The finding not only underscores the importance of this research model but also provides further support for the protective efficacy of the ML29 vaccine. In conjunction with the Institute of Human Virology at the University of Maryland, Dr. Patterson's group initially showed that this vaccine protected guinea pigs from a challenge with a lethal Lassa virus dose.

In other vaccine efforts, Dr. Patterson's research team has initiated studies with the Centers for Disease Control and Prevention to test a variety of flavivirus vaccines in rhesus monkeys. These DNA-based vaccines have shown to be safe while stimulating immune response in other animal systems. Now her laboratory has vaccinated animals with candidate vaccines to West Nile virus, Japanese encephalitis virus and dengue virus and, in the summer of 2007, will challenge the animals with the corresponding virus to test the vaccine's efficacy in preventing infection.

New weapon developed to battle the Texas-Mexico border threat of dengue fever. Dengue viruses are now transmitted in more than 100 countries by mosquitoes that are prevalent worldwide. Recently, this emerging virus has reached South Texas, with outbreaks every five years along the U.S. border with Mexico, particularly in Laredo, McAllen and Brownsville. Little is known about how the four different dengue viruses cause dengue fever – a flu-like disease – and its more severe form, dengue hemorrhagic fever, which causes massive bleeding. This is due to the fact that there has been no animal model to study dengue infection, since only humans show signs of disease.

But recent work by Dr. Rebeca Rico-Hesse and her laboratory has given researchers some effective new tools to better understand dengue and to test candidate vaccines and treatments for it. First, her research has identified the target cells of infection in the skin, enabling her to develop models of infection in human cell cultures from blood donors. Second, she has developed mice with humanized immune systems by transplanting them with human umbilical cord blood cells, which contain the target cells her group has identified as the sites of dengue virus replication in the human body. These advances have helped Dr. Rico-Hesse create the first animal model for dengue fever research, a major advance for drug companies waiting to test the efficacy of potential vaccines and anti-viral therapies.

Now Dr. Rico-Hesse's group is testing other strains of mice in order to obtain a better reconstitution of the human immune system to see if they can recreate severe dengue disease. The use of these mice, both in virus replication comparisons and in testing antivirals and potential vaccines, could help her laboratory determine which factors contribute the most to causing dengue hemorrhagic fever, and thus which viruses should be monitored for outbreak control throughout the world.

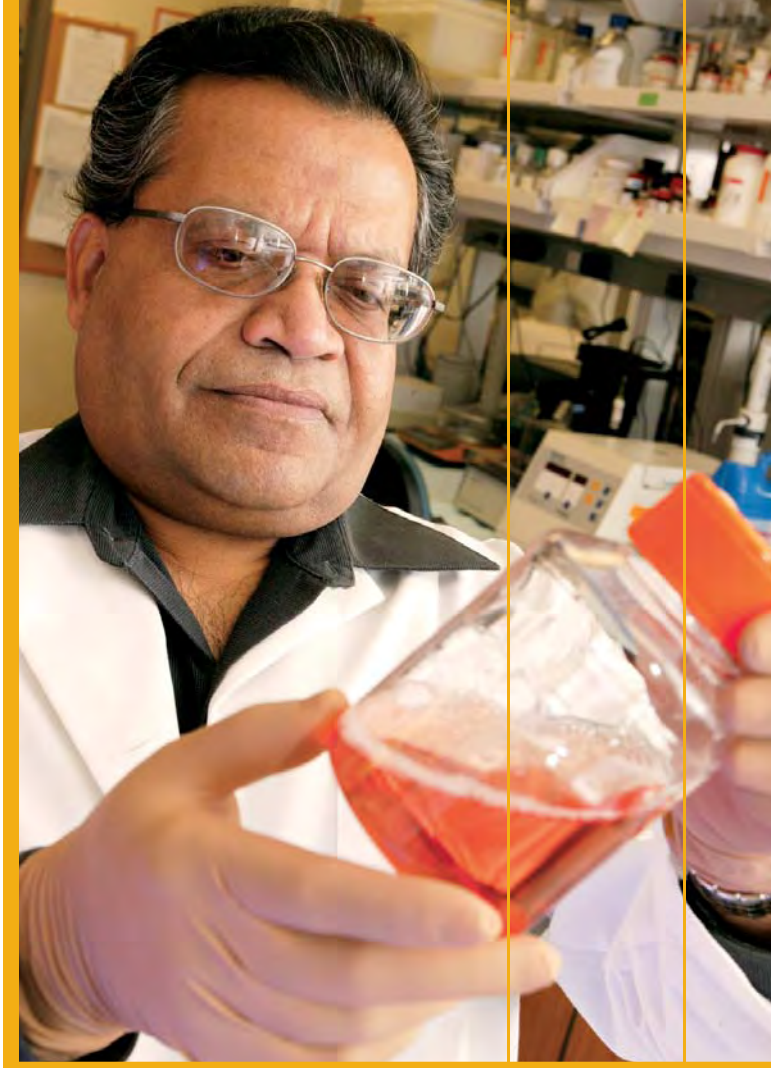
Building blocks for better biosensors. Llamas are an important part of Dr. Andrew Hayhurst's latest research, but not as research subjects. Rather, a few llama blood samples provided the source for Dr. Hayhurst to use his imagination and skill as an antibody engineer to build a unique library of more than 1 billion antibodies that are now being tested for their durability as well as their ability to detect various biothreat agents.

Llamas, like sharks and camels, have a rare type of antibody called a single-domain antibody (SdAb). These antibodies' unique properties make them more durable and heat-stable than conventional antibodies, as well as reusable, since SdAb can "refold" and return to their original shape after releasing an antibody to which they have bound. With this knowledge in mind, Dr. Hayhurst entered a collaboration with the Naval Research Laboratory to develop a large library of SdAb derivatives and test them to see if they could be incorporated into a new class of biosensor that is portable, reusable, able to withstand extreme field conditions such as high temperatures, and less expensive than current biosensors, providing a new biodefense resource with both military and civilian applications.

So far, the effort has been fruitful. Tests in SFBR's BSL-4 laboratory have shown antibodies from Dr. Hayurst's library to be effective in detecting biothreat agents such as the hemorrhagic fever viruses Marburg and Ebola. They also show the anti-Marburg SdAb to match conventional nucleic acid-based detection and sensitivity in a fraction of the time and expense.

Battling the modern plague of HIV/AIDS

While tremendous strides have been made in the treatment of HIV and AIDS over the past two decades, a cure or effective vaccine for this insidious virus remains elusive, to the detriment of people around the globe. The Joint United Nations Programme on HIV/AIDS reports that 40 million people worldwide were living with the disease in 2005. In the United States alone, according to the Centers for Disease Control and Prevention, more than 425,000 people were living with HIV in 2005, and there are approximately 40,000 new infections each year. This makes the development of a successful vaccine a public health priority.



Encouraging results with a DNA-based vaccine. At SFBR, Dr. Luis Giavedoni has been collaborating with researchers at Yale and Northwestern University to test the efficacy of a potential DNA vaccine that uses portions of the simian immunodeficiency virus (SIV), and the group has had some success.

After several inoculations with the vaccine, researchers did not see much of an immune response in rhesus monkeys, so they attempted to boost the animals' immunity with a vaccine based on a poxvirus – a type of AIDS vaccine that currently is in human clinical trials. Animals that received both vaccines responded more strongly than those that received only one, indicating that the DNA vaccine helps prime the immune system to enhance the effect of the pox-based vaccine. When Dr. Giavedoni challenged six animals that had received both vaccines with SIV, four were protected from infection. While these results are very encouraging, he and his collaborators are now working to modify the DNA component so that it stimulates an improved immune response with an even higher level of protection.

New type of "natural killer cells" identified. Dr. Krishna Murthy has been testing a humanized monoclonal antibody to the HIV receptor complex, or part of the immune cell's structure used by HIV to bind with and enter the cell. By binding with that receptor complex, the antibody blocks an essential mechanism needed by HIV to infect a cell, and if it cannot infect the cell, the virus eventually dies. This makes the monoclonal antibody a promising component of potential vaccines and new treatments for HIV and AIDS.

As part of these tests, Dr. Murthy and his research team have identified a novel subset of natural killer cells – a type of immune cell that targets tumor cells and protects against a wide variety of infectious microbes – that appears to play an important role in controlling HIV infection following activation by the cytokine IL-15 and induction of interferon gamma. Additional studies are underway to confirm and extend these observations. If the role of these natural killer cells in fighting HIV infection can be better understood, it could potentially be applied to new methods of treatment or to potential vaccines.

Better understanding of differing viral strains. Part of Dr. Jon Allan's work over the past year has focused on a simian (nonhuman primate) version of the AIDS virus called SIVagm as he has tried to understand how different strains of the virus differ in their infection patterns and ultimately the nature and course of disease they cause. His studies in the pigtailed macaque monkey model showed that lymphotropic strains – those infecting the immune system – had an accelerated pattern of replication and higher peak viral loads compared to a neurotropic strain (one infecting the brain). His findings indicate that lymphotropic strains overwhelm the infected animal's defenses and are thus more likely to cause disease in this simian model. He expects these findings to have broad implications as to how specific strain differences in HIV might influence disease outcome in humans.

New faculty member adds additional expertise. In 2006, the Department of Virology extended the depth and breadth of its programs on HIV and AIDS by welcoming Dr. Marie-Claire Gauduin as a new member of the faculty. Formerly an instructor at Harvard Medical School, Dr. Gauduin brought to SFBR her research program focused on the sexual transmission of HIV – which accounts for the majority of new infections worldwide – using the macaque model. In conjunction with the Pasteur Institute, she is examining the early mechanisms of viral transmission to explore the type and function of cells first infected, the pathways used by the virus to spread, and early immune responses at the viral site of entry. Her laboratory also is focusing on the neonatal monkey model of pediatric AIDS to understand the early immune responses against HIV and evaluate the efficacy of candidate vaccines in newborn and infant primates.

Striving to curb the hepatitis C epidemic

Hepatitis C virus (HCV) causes lifelong chronic liver disease in over 170 million people with slow progression to end-stage liver disease, cirrhosis, and liver cancer. HCV is the leading cause of liver transplantation and an increasing cause of liver cancer in the United States.

Uncovering why some people respond to HCV therapy and others do not. Currently, the only FDA-approved treatment is interferon-alpha (IFNα) plus ribavirin, a treatment of 24-48 weeks with severe side effects and a cure rate of less than 50 percent. IFNα works by turning on host genes that combat viral infections.

To better understand the reasons why some people fail to respond to IFNα therapy, Dr. Robert Lanford and his research team examined the effects of human and chimpanzee IFNα in the chimpanzee using a microarray chip containing a copy of every gene in the human genome. Dr. Lanford's laboratory was one of the first to use this method to examine infectious diseases.

In uninfected chimpanzees, Dr. Lanford detected over 1,000 genes that are induced by IFNα; however, no genes were induced in the liver of chimpanzees chronically infected with HCV, and the animals were completely resistant to the antiviral effects of IFNα. He also examined the genes induced in white blood cells, and they were very similar in both uninfected and HCV-infected chimpanzees. This indicated that some change had occurred in the liver of chimpanzees during chronic HCV infection that renders them resistant to IFNα. Dr. Lanford believes chimpanzees may mimic the group of humans referred to as null responders to IFNα. Further studies of the

chimpanzee may help researchers understand why IFNα therapy fails many people and how to improve the therapy for the future.

In pursuit of a vaccine for schistosomiasis

Schistosomiasis, a sometimes fatal parasitic disease that afflicts more than 200 million people in 76 countries around the globe, is one of the major causes of illness in the world today. Although medication is available to successfully treat the infection, it does nothing to prevent re-infection, a common problem in areas of the world where people are consistently exposed to the parasite through their environment. This makes the development of a vaccine critical to public health efforts.

At SFBR, Dr. Philip LoVerde runs one of the world's largest research programs on schistosomiasis, with studies aimed at discovering molecular mechanisms involved in interactions between the schistosome parasite and its host, or the person or animal it infects. His research has shown that adult schistosome worms are able to evade the host immune response by the use of antioxidant enzymes. Using naked DNA vaccines, Dr. LoVerde and his research team have demonstrated that forms of superoxide dismutase and glutathione peroxidase consistently provide significant protection against schistosome infection. They also have demonstrated for the first time that adult worms, not just the larval stages of the parasite, can be a target for immune elimination. This has resulted in a major advance in schistosome vaccine research, as previous studies have always focused on the larval stage as an immune target. Currently, Dr. LoVerde's laboratory is evaluating the efficacy of three vaccine candidates in baboons as a prelude to human clinical trials.

In collaboration is with The Institute for Genomic Research (TIGR) and the Wellcome Trust-Sanger Institute, Dr. LoVerde's team also has produced more than 8X coverage of the *S. mansoni* genome. The group is currently assembling and annotating the genome for publication.

New program aims to discover what makes herpes B deadly

After finishing his postdoctoral training at Harvard Medical School, Dr. Anthony Griffiths joined the SFBR Department of Virology and Immunology in 2006, bringing with him a new research program investigating why two viruses that are so similar – herpes simplex virus (HSV) and herpes B virus – have such a different impact on human health. HSV, to which most people are exposed by adulthood, is the cause of cold sores in humans. It is usually self-limiting and not life-threatening. On the other hand, herpes B virus, while fairly benign in macaque monkeys, is one of the most dangerous human pathogens known, causing death in 70 percent of those infected.

In his effort to discover why this is, Dr. Griffiths is gaining some important insights that go beyond herpes and may also be applied to other research fields. He is focusing primarily on a newly described class of molecules called microRNAs, which are powerful regulators of gene expression, because he believes the herpes B virus-encoded microRNAs are responsible for the strikingly different outcomes of herpes B infection in macaques and humans. In collaboration with Dr. Xiu-Jie Wang's laboratory at the Chinese Academy of Sciences, he has developed a computational method to predict microRNAs that may be encoded by herpes B. Out of 16 potential "hits," he has shown that three are present in herpes B-infected cells. He is currently investigating the functions of these microRNAs to see if they are the potential Achilles' heel of herpes B that could be the targets of a potential cure for this disease.

2006 Doctoral Staff

(as of December)

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Luis D. Giavedoni, Ph.D.
Robert E. Lanford, Ph.D.
Philip T. LoVerde, Ph.D.
Krishna K. Murthy, D.V.M., Ph.D.
Rebeca Rico-Hesse, Ph.D.

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Marie-Claire Gauduin, Ph.D.
Andrew Hayhurst, Ph.D.

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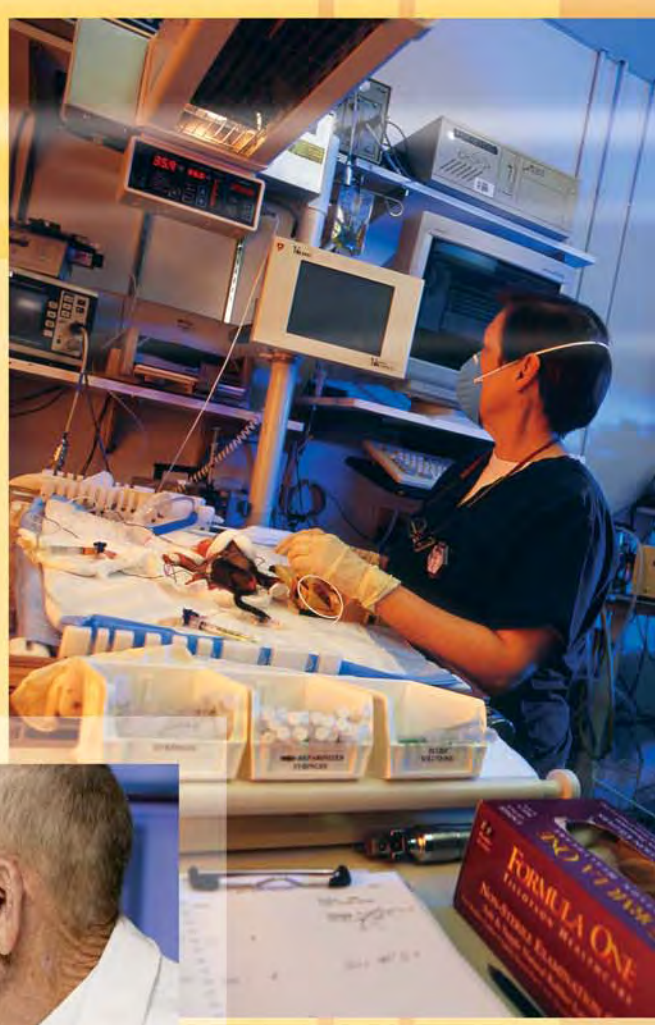
Department of Physiology & Medicine



Research in the Department of Physiology and Medicine

focuses on two of the top killers in the United States – cardiovascular disease and cancer – and health problems that affect the most defenseless among us, premature newborns. In their extensive collaborations with fellow faculty at SFBR, with the Foundation's Southwest National Primate Research Center, and with colleagues at other institutions throughout the United States and abroad, departmental scientists achieved several key advances in each of theses areas during 2006.

Cancer Drug Discovery

Recognizing that not all cancers respond to the same drugs, that not all patients respond the same way to the same drug, and that chemotherapy is a difficult treatment with devastating side effects of its own, Dr. Susan Mooberry is continually searching for new and less toxic ways to fight cancer. In this effort, she leads a cancer drug discovery program at SFBR in which she evaluates natural products, synthetic analogs of natural products and synthetic compounds *in vitro* (in cell cultures) for their ability to kill cancer cells. In particular, she examines the compounds' effects on cellular structures called microtubules, which are important in controlling cell division. For successful cell division, microtubules need to be dynamic. When the dynamics of microtubules are disrupted, the cell recognizes that something is inherently wrong and initiates a cellular suicide program. Dr. Mooberry's research program has identified several compounds that disrupt microtubules, and subsequent tests have shown that some might be good candidates for potential new cancer drugs.

One example identified in 2006 is CB694, which was found by screening a 10,000-synthetic-compound chemical library. CB694 was shown to disrupt microtubules by a process called depolymerization. Subsequent tests using tissue cultures of cancer cells have indicated that it inhibits proliferation of a wide range of cancer cell types and that it has the ability to avoid a major cancer mechanism that promotes multidrug resistance. In mouse models of cancer, CB694 was an effective antitumor agent.

Dr. Mooberry's research program continues to evaluate the laulimalides, a class of microtubule stabilizers first identified in her laboratory. In collaboration with Dr. Paul Wender at Stanford University, she has identified portions of the laulimalide molecular structure that are important for optimal biological activity. She and Dr. Wender also found that some laulimalide analogs have advantages over the natural compound for the ability to act together with other drugs to kill tumor cells.

This drug discovery program also continues to screen a variety of natural products that are extracted from marine organisms. Collaborations with the Grewick laboratory at the Scripps Institute of Oceanography and Dr. Diaa Youssef at Suez Canal University in Egypt identified new several cytoskeletal disrupting agents isolated from marine life, including red algae, cyanobacteria and sponges.

Cardiovascular Diseases

Advances in research on atherosclerosis. In 2006, the cardiovascular research programs within the Department of Physiology and Medicine produced two new findings in research on atherosclerosis, or hardening of the arteries. Using baboons in the pedigreed baboon colony maintained by the Southwest National

Primate Research Center, Dr. Rampratap Kushwaha conducted studies to test whether an enzyme found in liver and intestinal cells, 27-hydoxylase, was responsible for the increases in blood cholesterol levels that occur in response to a high-fat, high-cholesterol diet. His studies have shown that baboons with low levels of 27-hydroxylase in their liver cells are high responders to dietary fat and cholesterol. Additional observations suggest that 27-hydroxlase increases cell membrane transporters that may be important in the removal of cholesterol by bile secretions.

Another major development in atherosclerosis research was the result of two national collaborations with human research subjects. This latest development involved Dr. Henry C. McGill Jr. of SFBR and Dr. C. Alex McMahan of the University of Texas Health Science Center at San Antonio – two primary investigators in the national Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study – and investigators in the currently active Coronary Artery Calcium in Young Adults (CARDIA) study.

The PDAY study investigators had constructed a scoring system based on various risk factors for atherosclerosis and cardiovascular disease, including blood pressure, cholesterol and blood glucose levels, as well as smoking and obesity. The scoring system is designed to help clinicians assess their patients' risk for cardiovascular disease and is based on estimates of the contribution of each of these factors to blood vessel lesions observed in autopsy samples taken from young adults who died as victims of accident or homicide.

The CARDIA study assessed coronary artery calcium in living young adults who had been participating in this study for 15 years. Then PDAY risk scores for these subjects were calculated based on data collected at years 0, 5, 10, and 15 of the study. Analysis of this data revealed that the PDAY risk scores accurately predicted coronary artery calcification 10 to 15 years later. Furthermore, an increase in the PDAY risk score over time was associated with increases in coronary artery lesions, and decreases in risk scores over time were associated with a decreased risk of coronary artery disease. Therefore, this study supports the original hypothesis of the PDAY study, which is that lifestyle modifications early in life can have a significant impact on the development of cardiovascular disease as an adult. Researchers say it provides clear evidence that heart disease prevention needs to start in childhood. The study also affirms the effectiveness of the PDAY risk score system in helping physicians identify at-risk youth who require preventive interventions.

Salt-sensitive hypertension research. One focus of Dr. Robert Shade's research is the effect of sodium on blood pressure levels, and in particular, why sodium intake elevates some individuals' blood pressure more than others. His goal is to develop methods to help identify individuals at risk of developing salt-sensitive hypertension later in life and to devise strategies to help prevent it. His research in this area uses a biochemical marker of cell membrane sodium transport, red blood cell sodium-lithium countertransport (SLC), to identify baboons that are high or low for SLC. Humans with high SLC have been shown to have inherited salt-sensitive hypertension.

In collaboration with Dr. Laura Cox in the SFBR Genetics Department and researchers at Michigan State University, Dr. Shade established in 2006 that baboons with high SLC values and on a high-salt diet experience

an increase in blood pressure measured over 24-hour intervals when compared to baboons with normal SLC values. Now gene expression studies on kidney samples collected from baboons on low- and high-salt diets are under way in an effort to identify the genes or gene pathways that contribute to this high SLC phenotype that is a precursor of salt-sensitive hypertension.

Diseases of premature birth

A truly unique resource at SFBR is a neonatal intensive care unit for premature baboons, which are prone to premature lung disease and other health and developmental problems faced by human infants who are born prematurely. Over the years, research with this animal model at SFBR has led to several important medical advances in the rescue and most effective care of the tiniest of infants, and today, investigators from San Antonio and around the world collaboratively use this extraordinary resource to achieve further advances in this field.

In 2006, the Foundation's NICU supported 10 research programs that had an overall focus on the molecular mechanisms that contribute to the development of lung disease caused by premature birth. These projects provided new information on the roles of vitamins, hormones, and biochemical agents that promote lung maturation as well as lung injury or repair. In particular, this research has shown that premature birth induces inflammatory processes in lung tissue that contribute to the lung disease that can persist in adult survivors of premature birth. Therefore, NICU researchers hope to define preventive measures that can be used both to save the lives of premature infants and improve their lifetime health by investigating various approaches to reduce lung inflammation. These include methods of preventing airway infection, reducing oxygen concentration during artificial ventilation procedures, and providing antioxidant treatment.

Many thanks go to Dr. Jacqueline Coalson, an adjunct scientist at SFBR and pathologist at the University of Texas Health Science Center at San Antonio, who has served for many years as the principal investigator for the NICU programs. Upon her retirement, Dr. Don McCurnin, an SFBR adjunct and UTHSCSA faculty member who serves as the medical director for the NICU, will step into this vital leadership role.

2006 Doctoral Staff

(as of December)

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Senior Scientist Emeritus
Henry C. McGill Jr., M.D.

Scientist
Rampratap S. Kushwaha, Ph.D.

Associate Scientist
Susan L. Mooberry, Ph.D.

Department of Organic Chemistry

In April 2006, the Department of Organic Chemistry entered into year five of a five-year contract as The Synthetic Chemical Facility for the Contraceptive Development Branch (CDB) of the National Institute of Child Health and Human Development, National Institutes of Health. This marks the 30th consecutive year that the department has served in this capacity through a number of contracts.

These contracts are awarded on a competitive basis, and the Department of Organic Chemistry has been consistently recognized as the premier research group in the nation for steroid synthesis. Over the years, Department Chair and Senior Scientist Dr. P.N. Rao and his research group have developed synthetic methods for the production of hundreds of steroids and other compounds. These compounds have been investigated for development of safer and more effective methods of contraception as well as for the treatment of a variety of reproductive disorders.

Current projects and areas of research interest include:

Selective progesterone receptor modulators

The potential applications of selective progesterone receptor modulators involve contraception as well as treatment of endometriosis, progesterone-dependent tumors, uterine fibroids, premenstrual syndrome, and adverse symptoms of menopause.

The antiprogestin known as CDB-4124 was conceived and synthesized in Dr. Rao's laboratories. Subsequent biological testing indicated this analog exhibited three times the antiprogestational activity of the parent compound with significantly decreased side effects. This compound and 48 other derivatives are the subject of two U.S. patents awarded to scientists in the Department of Organic Chemistry in 2005.

Under the trade name Proellex™ (formerly known as Progenta™), CDB-4124 has been licensed to Repros Inc. (formerly Zonagen Inc.) for development in the treatment of uterine fibroids and endometriosis, as well as progesterone-dependent breast tumors. In late 2004, Repros Inc. completed a European Phase 1b clinical study of Proellex™ in women with uterine fibroids. Results released by Zonagen Inc. in 2005 indicate that Proellex™ is well tolerated with no undue side effects, and it achieved statistically significant reduction in fibroid size compared to a control group. Proellex™ also performed favorably when compared to a positive control group using Lupron®, a GnRH agonist commonly administered for the treatment of fibroids. In late 2005, Repros Inc. received approval to initiate a U.S. Phase 2 trial for the study of Proellex™ in the treatment of uterine fibroids, which is currently ongoing.

Also in late 2005, Repros Inc. received approval to start a European Phase 2 study of Proellex™ for the treatment of endometriosis. Preliminary results from the endometriosis study announced in December 2006 indicate that treatment with Proellex™ achieved significant pain reduction when compared to treatment with Lupron®, the current pharmaceutical standard of care for the treatment of endometriosis. Interim results indicate side effects of Proellex™ were generally mild with no indication of toxicity or endometrial hyperpla-

sia. Pending final results of this European study, Repros Inc. anticipates submitting an investigational new drug application to the Food and Drug Administration to initiate a Phase 2/3 study of Proellex for the treatment of endometriosis in the United States. Pending clearance of the IND, Repros Inc. anticipates commencing this trial in the second quarter of 2007.

Male contraceptives

One promising approach to controlling male fertility is through the administration of a single agent that is both antigonadotropic and androgenic. It has been reported that several derivatives of 19-nortestosterone are more potent than testosterone with a longer duration of action. Over the past year, Dr. Rao and his research team have synthesized several novel derivatives of 19-nortestosterone that will be tested as male contraceptives. The group also completed a relatively large-scale synthesis of 11β-methyl-19-nortestosterone 17β-dodecylcarbonate under the FDA's current Good Manufacturing Practice (cGMP) regulations to provide the National Institutes of Health with material suitable for future clinical studies.

Another method for controlling male fertility involves a recent investigation into reversible infertility in male mice induced by oral administration of certain N-alkylated imino sugars. This study represents a potential nonhormonal approach to male contraception. Over the past year, the department has synthesized a novel N-alkylated imino sugar to be studied by NIH in animal models.

Radiolabeled syntheses

Very often, investigations into potential and existing pharmaceuticals require the use of radiolabeled analogs for metabolic, enzymatic and radioimmunoassay procedures. Over the past year, Dr. Rao's laboratory has prepared two such analogs, tritiated 11β-methyl-19-nortestosterone and tritiated Levonorgestrel, both to be used by NIH for biological investigations.

Novel 2-methoxyestradiol compounds with anticancer activity

2-Methoxyestradiol (2-ME2) is a natural metabolite of estradiol devoid of estrogenic or tumor-promoting activity *in vivo*. In 1989, it was discovered that 2-ME2 inhibits the cellular machinery involved in replicating cancer cells, specifically microtubules, the intracellular target of the well known anticancer drug Taxol™. In addition, 2-ME2 has been demonstrated to act as an antiangiogenic agent that prevents the growth of new blood vessels required to nourish tumors. Upon learning these findings, the Department of Organic Chemistry initiated a program to investigate the potential anticancer application of prior and newly synthesized 2-ME2 derivatives. These compounds were tested for antiproliferative activity against breast and ovarian cancer cells *in vitro*, and three of the analogs were found to have promising activity.

The compounds and methods developed in Dr. Rao's laboratories for the synthesis of these analogs are the subject of two U.S. Patents awarded to Southwest Foundation for Biomedical Research.

Over the past year, the Department of Organic Chemistry has synthesized several new analogs of 2-ME2, which have been tested by EntreMed Inc. of Rockville, Md. Preliminary results from *in vitro* testing indicate five new compounds with promising results, one of which, known as RC-57, is being tested in an animal model by EntreMed Inc.

2006 Doctoral Staff

(as of December)

Senior Scientist and Chair
Pemmaraju N. Rao, Ph.D.

Southwest National Primate Research Center

A true gem among the Foundation's unique collection

of extraordinary resources, the Southwest National Primate Research Center (SNPRC) is a vital national resource that serves scientists at major research institutions from across the country. It is one of only eight National Primate Research Centers funded by the National Institutes of Health to facilitate critical biomedical research efforts that require primate models of human disease. Each center offers particular specialties in scientific expertise and animal resources for the benefit of research at its host institution and with collaborators nationwide.

The SNPRC was made part of the NIH network of primate centers in 1999 in recognition of the Foundation's long and distinguished history in research with nonhuman primates, making it the first new center to be established since the program's inception 40 years earlier. The youngest center in the program, the SNPRC has brought specialized expertise in genetics and virology to the National Primate Research Centers Program in addition to its world-class primate resources.

The SNPRC supports an active and diverse range of research with nonhuman primates, conducted both by internal investigators at SFBR and external investigators at collaborating institutions. In 2006, the SNPRC provided research support to 109 investigators, 78 percent of whom were located at institutions other than SFBR. Collaborators included major biomedical research institutions within Texas, such as Baylor College of Medicine, the University of Texas at Austin, the University of Texas Medical Branch at Galveston, the University of Texas Southwestern Medical School, and the University of Texas Health Science Center at San Antonio, as well as top research institutions throughout the country, including the Scripps Clinic, the Salk Institute, Harvard Children's Hospital, Johns Hopkins University, and the University of California, San Francisco.

The breadth of research supported by the SNPRC is remarkable. SNPRC resources, including animals and unique technical expertises, played vital roles in studies of atherosclerosis, hypertension, obesity, diabetes, metabolic syndrome, osteoporosis, lumbar disc degeneration, epilepsy, sickle cell anemia, non-Hodgkin's lymphoma, behavioral and psychiatric disorders, prenatal and neonatal disease, aging, tuberculosis, Lassa fever, West Nile fever, equine encephalitis, pneumonia, influenza, periodontitis, hepatitis B and C, HIV/AIDS, and bioterrorism agents.

Improving human health by facilitating research with nonhuman primates

The mission of the SNPRC is to improve the health of our global community through innovative biomedical research with nonhuman primates. This mission statement parallels the SFBR mission statement and emphasizes the international role of our primate center in facilitating biomedical research and contributing to solving the world's most pressing health concerns. Many research programs can only be conducted successfully using nonhuman primates, since no other animals so completely share the complex physiological and disease-related processes that are critical to understanding the pathogenesis of complex and infectious diseases. Many investigations rely on the detailed study of a whole, living system. As the animals most biologically similar to humans, nonhuman primates serve as the gold standard for research in this area. The close relationship between humans and nonhuman primates also means that genes found to be important for determining differential susceptibility to disease in monkeys will also have significant effects in humans.

The SNPRC maintains several uniquely characterized colonies of nonhuman primates for use in combating the diseases that threaten humanity because

adequate treatments or preventions are lacking. The baboon colony at SFBR is the largest in the world and provides a unique colony of pedigreed animals for genetic research on a broad range of chronic diseases and physiological traits. The chimpanzee colony is also one of the largest available to researchers and is highly utilized for hepatitis and AIDS research, as well as for developing novel therapeutics for both infectious and noninfectious human diseases. On December 31, 2006, the SNPRC's nonhuman primate colonies comprised 5,700 animals, including baboons, macaques, chimpanzees and marmosets.

Establishing high biocontainment research capabilities

After several years of planning and construction, the SNPRC opened a new animal biosafety level 3 (ABSL-3) facility during 2006. This facility is important to biodefense and other research programs on infectious diseases because it provides the space and high level of biocontainment necessary to conduct nonhuman primate studies safely with almost any of the dangerous viruses and bacteria that cause disease in humans. This makes the ABSL-3 vital to preclinical trials on new vaccines and drug therapies for some of the most dangerous pathogens facing humanity. During 2006, two studies were conducted in the ABSL-3 on pathogens considered to be major threats to human health. One was an assessment of anthrax as a food-borne bioterrorist threat. The other was aimed at developing a vaccine for West Nile virus, a serious mosquito-borne disease that is occurring in the United States with increasing frequency.

In 2007, the ABSL-3 facility will be used in an exciting new project designed to develop a new vaccine for tuberculosis. Tuberculosis is the leading cause of death from a single microorganism. Approximately 9 million people worldwide develop TB each year, and 2 million people die of the disease annually. Drug resistance has increased dramatically in recent years, making treatment of TB problematic. A more effective vaccine is desperately needed for this disease, and the nonhuman primate resources of the SNPRC will play a critical role in the testing and development of this novel approach to TB control.

Managing primate resources

In addition to meeting the daily demands of the animals' physical care and enrichment needs, members of the SNPRC veterinary and technical staff perform a variety of observational procedures and research protocols in support of research projects by SFBR and other collaborating scientists. Veterinary staff members also conduct

research concerned with health problems in the nonhuman primate colonies and search for spontaneous nonhuman primate models of human disease.

A critical function of SNPRC staff is to ensure that all the Foundation's animal programs are in compliance with state and national regulations, federal regulatory agencies, and voluntary accrediting agencies. Since 1973, SFBR has been accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care, International (AAALAC, Int.), an agency that assures high-quality standards for the care and use of laboratory animals.

Supporting investigators in groundbreaking research

The SNPRC has provided resources that formed the base of many of the most exciting accomplishments of SFBR scientists and their collaborators during 2006. In fact, the SNPRC 2006 report of progress submitted to the NIH listed 75 publications in the international scientific literature. Following are a few highlights of the accomplishments those publications reported:

Nonhuman primate gene maps. SNPRC investigators published an initial gene map of the rhesus monkey and a second-generation gene map of the baboon. These maps are essential to investigators at SFBR and many other institutions for gene discovery research programs. Using these gene maps in conjunction with the human gene map enables scientists to pinpoint the chromosomal locations of specific genes that influence disease processes, and then to identify those genes and to determine their mechanisms of action.

B-cell lymphoma. B-cell or non-Hodgkin's lymphoma (NHL) is caused by the proliferation of malignant (cancerous) B-cell lymphocytes in the blood and represents 85 percent of lymphomas in the United States. The lifetime risk of being diagnosed with NHL in this country is 2.08 percent, and the incidence rate is increasing by 3 percent per year. Investigators from two German institutions and SFBR published a report that establishes the safety and efficacy of a monoclonal antibody to deplete the excess of B-cells in people who have NHL. The antibody was tested at the SNPRC in chimpanzees, and it is now being tested in a clinical trial with human patients.

Hypertension. Hypertension, or high blood pressure, is a major cause of cardiovascular disease and stroke, our nation's bigger killers. Investigators from the University of Texas Health Science Center at San Antonio, in collaboration with SFBR investigators, published their finding that mild nutrient restriction in pregnant baboons impairs kidney development in the fetus, making the offspring more susceptible to hypertension as they become adults. This finding emphasizes the importance of efforts to ensure that women get adequate nutrition during pregnancy.

2006 Doctoral Staff

(as of December)

Director
John L. VandeBerg, Ph.D.

Interim Associate Directors, Research Resources
Luis D. Giavedoni, Ph.D.
Jeffrey A. Rogers, Ph.D.

Associate Director, Veterinary Resources
L. Bill Cummins, D.V.M.

Other Core Scientists
Jonathan S. Allan, D.V.M.
Raul A. Bastarrachea-Sosa, M.D.
Kathleen M. Brasky, V.M.D.
Stephanie D. Butler, D.V.M., M.S.
Anthony G. Comuzzie, Ph.D.
Laura A. Cox, Ph.D.
Melissa A. de la Garza, D.V.M.
Edward J. Dick Jr., D.V.M.
Vida L. Hodara, Ph.D.
Gene B. Hubbard, D.V.M.
Robert E. Lanford, Ph.D.
Corrine Lutz, Ph.D.
Michael C. Mahaney, Ph.D.
Krishna K. Murthy, D.V.M., Ph.D.
Jerilyn K. Pecotte, Ph.D.
Karen S. Rice, Ph.D.
Robert E. Shade, Ph.D.
R. Mark Sharp, Ph.D.
Suzette D. Tardif, Ph.D.
Jeff T. Williams, Ph.D.

Staff Scientists
Jeannie Chan, Ph.D.
Nicolas Gouin, Ph.D.
James Mubiru, Ph.D.
Qiang Shi, Ph.D.

New Grants and Contracts Awarded in 2006

Federal Research Grants and Contracts

	Length of Grant	Total Amount to SFBR
NIH *Strong Heart Family Study* Dr. Jean MacCluer, principal investigator	4 years	$4,104,280
NIH/NIMH *Quantitative Trait Locus Mapping in Human Pedigrees* Dr. John Blangero, principal investigator	5 years	$3,852,162
NIH/NIMH *Genetics of Brain Structure and Function* Dr. John Blangero, principal investigator	5 years	$3,583,578
NIH/NICHD *Identification of Preeclampsia Susceptibility Genes* Dr. Eric Moses, principal investigator	5 years	$2,342,230
NIH *Mapping Drug Resistance Genes in Plasmodium falciparum* Dr. Timothy J.C. Anderson, principal investigator	5 years	$2,301,287
NIH/NHLBI *Genetics of Infection and its Relationship with CVD Risk* Dr. Harald H.H. Göring, principal investigator	4 years	$1,911,684
NIH/NCRR *Luminex Technology for the Quantification of Cytokines in Non-human Primates* Dr. Luis Giavedoni, principal investigator	4 years	$1,710,000
NIH/NIAID *Dengue Virus Determinants of Virulence and Transmission* Dr. Rebeca Rico-Hesse, principal investigator	4 years	$1,660,000
NIH/NCI *Taccalonolides: Mechanisms of Action and Cellular Resistance* Dr. Susan Mooberry, principal investigator	5 years	$1,497,501
NIH *Replicative Fitness of SIV Variants* Dr. Jason Kimata, Baylor College of Medicine, principal investigator Dr. Jonathan Allan, SFBR, co-investigator	4 years	$ 711,358

	Length of Grant	Total Amount to SFBR
NIH/NCRR *Southwest National Primate Research Center – Supplement* Mr. John C. Kerr, principal investigator Dr. John L. VandeBerg, director	9 months	$638,690
NIH *NIDDM Susceptibility Genes in Mexican Americans* Dr. Michael Stern, University of Texas Health Science Center at San Antonio, principal investigator Dr. Harald H.H. Göring, principal investigator on subcontract to SFBR	5 years	$611,097
DOD/Navy Engineering Logistics Office *Task 2079, Foodborne Threat Assessment* Dr. Jean Patterson, principal investigator	1 year	$542,059
NIH/NHLBI *Maintenance of Chimpanzees for Hepatitis and AIDS Research – Supplement* Dr. Krishna Murthy, principal investigator	5 months	$466,117
NIH/NCRR *Bridge Funding for Rhesus Macaques* Dr. Larry B. Cummins, principal investigator	4 months	$353,189
NIH/NCRR *Southwest National Primate Research Center – Supplement* Mr. John C. Kerr, principal investigator Dr. John L. VandeBerg, director	9 months	$179,000
NIH *Induced Islet Neogenesis Therapy in Vivo* Dr. Lawrence Chan, Baylor College of Medicine, principal investigator Dr. Karen Rice, SFBR, co-investigator	1 year	$168,546
NIH *Nutrient Restriction and Developmental Programming* Dr. Peter Nathanielsz, University of Texas Health Science Center at San Antonio, principal investigator Dr. Karen Rice, principal investigator on subcontract to SFBR	1 year	$163,399
NIH/NCRR *Research Supplement to Promote Diversity in Health-Related Research – Southwest National Primate Research Center* Mr. John C. Kerr, principal investigator Dr. John L. VandeBerg, director	2 years	$138,433
NIH *Regional VI Center for Biodefense and Emerging Infections: New Opportunities* Dr. Jean Patterson, principal investigator	1 year	$134,704

Continued on page 36

Continued from page 35

	Length of Grant	Total Amount to SFBR
DOD/Naval Research Laboratories *Development and Testing of Recombinant Single Domain Antibodies* Dr. Andrew Hayhurst, principal investigator	10 months	$ 123,954
Miscellaneous federal grants and contracts (under $100,000 each)		$ 494,066
Total Federal Research Grants and Contracts		**$27,687,334**

Commercial Research Contracts

Commercial contracts greater than $100,000 (8):		$ 3,056,849
Miscellaneous commercial contracts less than $100,000 (29):		$ 965,298
Total Commercial Contracts		**$ 4,022,147**

Research Grants from Philanthropic Donors

Robert J. Kleberg Jr. and Helen C. Kleberg Foundation *Monodelphis Research Program* Dr. John L. VandeBerg, principal investigator	1 year	$ 358,400
The Hearst Foundation, Inc. *Pre-clinical Development of New Anti-cancer Agents* Dr. Susan Mooberry, principal investigator	1 year	$ 200,000
Cystinosis Research Foundation, NATALIE'S WISH *Complex Genetic Approaches to Monogenic Disease: Genomic and Transcriptonic Dissection of Normal Expression of CTNS, the Gene Involved in Nephropathic Cystinosis* Dr. Eric Moses, principal investigator	2 years	$ 148,535
Elizabeth Huth Coates Charitable Foundation *Genetic Dissection of Cystinosis: An Innovative Program for Novel Mechanism/Gene Discovery* Dr. John Blangero, principal investigator	1 year	$ 46,320
San Antonio Area Foundation *Positional Candidate Gene Screening of Three Novel Pre-eclamptic Genomic Susceptibility Regions* Dr. Matthew Johnson, principal investigator	1 year	$ 34,972
San Antonio Area Foundation *Mitochondrial Determinants of Diabetes Risk* Dr. Joanne Curran, principal investigator	1 year	$ 34,909
Joe and Jesse Crump Fund for Medical Research *Cancer Drug Discovery and Development – Molecular Pharmacology of Microtubular Stabilizers* Dr. Susan Mooberry, principal investigator	1 year	$ 25,000

	Length of Grant	Total Amount to SFBR
Southwest Foundation Forum *Characterization of the Praziquantel Drug-resistant Phenotype in the Human Parasite Schistosoma mansoni* Dr. Charles Criscione, principal investigator	1 year	$ 25,000
Southwest Foundation Forum *Investigation of Herpes B Virus Encoded MicroRNAs* Dr. Anthony Griffiths, principal investigator	1 year	$ 25,000
Southwest Foundation Forum *The Common Marmoset (Callithrix jacchus) as a Model for Ebola Hemorrhagic Fever* Dr. Ricardo Carrion Jr., principal investigator	1 year	$ 24,981
Southwest Foundation Forum *Characterization of Immune Cell Populations in the Circulation and Adipose Tissue of Healthy Baboons by Flow Cytometry: A Novel Class of Quantitative Phenotypes Linking Inflammation to Obesity* Dr. J. Michael Proffitt, principal investigator	1 year	$ 24,703
Southwest Foundation Forum *Genome-wide Differential Gene Expression in Profiling for the Identification of Preeclampsia Susceptibility Genes* Dr. Matthew Johnson, principal investigator	1 year	$ 24,118
Southwest Foundation Forum *Functional Brain Imaging in Baboons* Dr. Jeffrey Rogers, principal investigator	1 year	$ 22,418
Richard and Dianne Azar Fund *Genetic Dissection of Cystinosis: An Innovative Program for Novel Mechanism/Gene Discovery – Supplement* Dr. John Blangero, principal investigator	1 year	$ 14,125
Shelby Rae Tengg Foundation *Cancer Drug Discovery* Dr. Susan Mooberry, principal investigator	1 year	$ 10,000
Helen Freeborn Kerr Foundation *Cancer Drug Discovery* Dr. Susan Mooberry, principal investigator	1 year	$ 9,500
Total Philanthropic Grants[1]		**$ 1,027,981**
Total of New Grants and Contracts Awarded in 2006		**$32,737,462**

[1] Additional philanthropic grants were awarded in 2006 in support of ongoing research. The granting institutions and their gift amounts are as follows:

George W. Brackenridge Foundation Support of Educational Assistance for Postdoctoral Fellowships at the Southwest Foundation for Biomedical Research	$110,000
The Edouard Foundation, Inc. LightCycler Unit for Maximum Containment Laboratory	$ 27,000
Dickson-Allen Foundation *Genetic Effects on Bone Strength: Identifying Genes that Lead to Osteoporosis Risk* Dr. Lorena Havill, principal investigator	$ 20,000

Why Support SFBR?

It's a fact of life that grants and other income do not provide all the resources SFBR needs to achieve its important mission. Since the organization's founding, giving has played the role of a powerful enabler of progress, making philanthropy one of the cornerstones of this institution. Here are a few examples of how your financial support can make all the difference to SFBR scientists:

Leverage. On average, for every $1 contributed, SFBR scientists gain another $8 in competitive grant support, making our researchers among the most productive anywhere.

Critical programs and projects. Research grant and contract funding is the majority funding source of SFBR, totaling about 75 percent of our revenue. The remaining support must come from endowment income and current donations.

Key research ventures. Donations fund recruitment of key scientists and pilot studies, each representing strategies that encourage bold initiatives by new and existing faculty.

Extraordinary resources. SFBR has a history of developing rare scientific resources. The AT&T Genomics Computing Center and the BSL-4 maximum containment laboratory are examples of such resources funded by donations.

Technology. Modern research is made more productive by the latest in technology. The higher cost of the newest technology usually requires philanthropic support.

Make the difference. Unlike some research organizations, SFBR must rely on donations as the sole source for funding new programs and capital. SFBR does not have patient or tuition revenue or direct governmental allocations to fund capital and operating expenses.

SFBR excels as a center for scientific research because of the philanthropic support of our donors. Will you consider becoming our partner in progress? In addition to donor opportunities highlighted in this report, such as the Golden Circle, The Argyle, Founder's Council and Southwest Foundation Forum, the Foundation offers opportunities for legacy gifts, capital and endowment gifts, and memorial and honor gifts.

For more information on any of these giving opportunities, contact SFBR's chief development officer, Mr. Corbett Christie, at 210-258-9870 or cchristie@sfbr.org, or visit our Web site at www.sfbr.org and click on "Support SFBR."

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