SNPRC Celebrates 10th Anniversary

The Southwest National Primate Research Center (SNPRC) celebrated its 10th anniversary on October 1, 2009 with a program highlighting the center's history and accomplishments in the areas of infectious diseases and biodefense, development and aging, chronic diseases and genomics.

Established in 1999, SNPRC became the first new National Primate Research Center (NPRC) in more than 35 years. The SNPRC brought a number of unique strengths to the NPRC program, stemming from a long, productive history of nonhuman primate research at its host institution, the Southwest Foundation for Biomedical Research (SFBR). It currently maintains approximately 3,700 primates.

“These unique strengths include the world’s largest research baboon population, the world’s largest and best-characterized pedigreed primate population, the world’s largest group of geneticists committed to research with and management of captive nonhuman primates and high level biocontainment and infectious disease research,” said John L. VandeBerg, Ph.D., SNPRC’s director.

Sessions during the October 1 event held at SFBR included comments from representatives of the National Institutes of Health (NIH), which funds the SNPRC base grant; officials of other primate centers; and current and former SNPRC leaders. NIH officials noted how much the “baby” of the primate centers program has accomplished in its first ten years, bringing expertise in genetics, bioinformatics, genetic management, and virology and biocontainment to the program.

Important Collaborations

Leaders at US primate centers from New England, Wisconsin, Wake Forest University, and Louisiana described how the collaborations with the SNPRC are critical for advancing research at their own institutions. William Stone, Ph.D., a mentor and close friend of VandeBerg, reviewed some of the major advances in human medicine based on research using chimpanzees, baboons and rhesus monkeys.

SNPRC provides broad collaborative opportunities in primate research to investigators across the nation, and serves the entire country with specialized technologies, capabilities, and primate resources, many of which are unique to the center.

While the SNPRC celebrated its 10th anniversary this year, SFBR scientists obtained their first research baboon by 1960, shortly after the discovery of fatty plaque in the aorta of a female baboon that died at the Audubon Park Zoo in New Orleans — providing scientists with their first good animal model for human heart disease. The population quickly grew and became an important scientific asset to the nation.

The federal government established seven national primate research centers during the early 1960s. SFBR applied for the designation but was not selected. Why it was not chosen was never clear. “I asked that question periodically of just about anybody who would listen, and I never got a satisfactory answer,” said VandeBerg, who pushed for years to have the Foundation added to the group.

In 1961, federal officials felt the baboon wasn’t completely established as a model for heart disease, said Jerry Robinson, Ph.D., who oversaw the primate program for NIH’s National Center for Research Resources (NCRR) from 1995 to 2004.

But in 1999, in part because the race for an AIDS vaccine required more primate research, the NIH solicited applications for another center. SFBR was ready and was awarded the designation.

SNPRC Accomplishments; Future

Among SNPRC’s many accomplishments are advancing the understanding of cholesterol metabolism; identifying genes that influence heart disease, obesity, and diabetes; and developing a widely used vaccine for hepatitis B and a high-frequency ventilator used to keep premature babies alive.

Moving into the future, Jack Harding, Ph.D., NCRR’s current director of primate resources, noted that the agency continues to emphasize the importance of translational research, one of SNPRC’s strengths. He also said that consortium-building among the NPRCs is important for them to be as effective as possible.

“We clearly recognize the absolute necessity of animal research,” said SFBR President Kenneth P. Trevett.

“Our primates are essential for medical progress, as are mice, rats, guinea pigs and opossums. Without them we would be stripped of the very tools we need to open new paths of discovery and to challenge old dogma.”
**A letter from the President and CEO**

Dear Friends,

I recently attended the annual meeting of the Association of Independent Research Institutes (AIRI), a group of 91 free-standing, not-for-profit biomedical and behavioral research organizations. These organizations get most of their support from the National Institutes of Health (NIH). Of interest is the fact that this small number of research institutes accounts for approximately 6 percent of the extramural awards granted by the NIH, out of a total number of grantees of over 2,300!

Clearly, the independent research institute environment is a highly productive one, and the scientists working in these organizations are making an extraordinary impact on biomedicine and healthcare in the United States and throughout the world. And each of you who either works at the Southwest Foundation or supports it as a volunteer or donor can be very proud that SFBR is among the leading organizations within this peer group — judged by manuscripts written and NIH dollars awarded.

However, a major factor distinguishing SFBR from many of the other independent biomedical research organizations within AIRI is a strong legacy of philanthropy — manifested by strong restricted and unrestricted annual giving, generous capital support, and a significant endowment. This support has allowed us to embark on new scientific initiatives, enhance our physical plant, purchase specialized instrumentation, recruit outstanding researchers and other personnel, maintain the truly unique combination of research resources we have on campus, and underpin the highly sophisticated research environment that exists here. Think of it: the Southwest Foundation Forum, Founder’s Council, and the Golden Circle all provide sustenance for a truly vibrant and diverse scientific effort. Those organizations which are not so fortunate as to have the committed and long-standing support of many donors are simply not able to provide this environment, and in certain cases, are facing drastic repercussions from the current economic situation. These include layoffs, salary reductions, postponement of capital projects, and sadly in two cases, bankruptcy.

Fiscal strength and revenue diversity are necessary prerequisites for continuing scientific excellence. We at SFBR are so grateful to each of you who volunteers time and money to make for a healthier future — in our neighborhoods and around the world. You are having an important impact on developing better methods for controlling tuberculosis, Type II diabetes, a variety of mental illnesses, AIDS, malaria, cancer, bioterrorist threats, and many other life-altering and life-threatening conditions.

We believe in hope at SFBR, that great minds, acting cooperatively and constructively, can alter the human and animal health status of our planet. That’s no small aspiration, but it is becoming a more achievable goal every single day.

Thank you for taking this journey with us. It is not always easy, but it is always important.

Kenneth P. Trevett

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**SFBR National Advisory Committee Members Announced**

SFBR President Kenneth P. Trevett has announced the membership of a new national advisory committee. It is comprised of individuals with excellent credentials and will meet annually to advise the SFBR board of trustees and management on strategic issues. Members include:

- Claude Bouchard, Ph.D., executive director of the Pennington Biomedical Research Center and holder of the George Bray Chair in Nutrition at Louisiana State University in Baton Rouge.
- Richard Doughty, M.S., C.M.A., associate director of administration at the Oregon Health Sciences University and Oregon National Primate Research Center.
- James LeDuc, Ph.D., a professor of microbiology and immunology and holder of Shope-Dunn Chair in Global Health, and associate director of the Galveston National Laboratory, at the University of Texas Medical Branch.
- Margaret Kripke, Ph.D., a professor of immunology and, until recently, executive vice president and chief academic officer at the M.D. Anderson Cancer Center in Houston.
- Robert Mahley, M.D., Ph.D., president of the J. David Gladstone Institutes and professor of medicine and pathology at the University of California at San Francisco.
- Kenneth Shine, M.D., executive vice chancellor for health affairs for the University of Texas System and professor emeritus and former dean of medicine at the University of California at Los Angeles, as well as provost for health sciences there.
SFBR Virologist Jonathan Allan Dies

World renowned virologist and AIDS expert Jonathan S. Allan, D.V.M., 57, passed away on September 27, 2009, following a courageous battle with brain cancer.

“Jon was a wonderful colleague and friend to his fellow virologists and immunologists, and will be very much missed by his department at SFBR,” said Jean L. Patterson, Ph.D., chair of SFBR’s Department of Virology and Immunology.

Added SFBR’s Chief Scientific Officer John L. VandeBerg, Ph.D.: “Jon always had a smile which accompanied his great sense of humor, he was always willing to help when asked, and he made exceptionally thoughtful and articulate contributions to the committees on which he served.”

Allan was an early pioneer in AIDS-related research with nonhuman primates. His research focused on the question of why African monkeys that carry SIV, the monkey form of HIV, remain healthy whereas Asian monkeys infected with SIV develop AIDS. A review of this topic, on which Allan was second author, appeared in the August 2009 issue of the prestigious journal, Nature Medicine (Towards an AIDS vaccine: Lessons from natural simian immunodeficiency virus infections of African nonhuman primate hosts. Nature Medicine 15:861-865, 2009).

Allan also was an author on numerous articles that dealt with transmission of viruses from nonhuman primates to humans. In the 1990s, he became an avid spokesperson against the use of baboons as donors of organs for transplantation into humans. He argued that the risk of zoonotic viral transmission from baboons to humans was great, and that viral mutations could lead to new pandemics such as AIDS. His position was controversial, and unpopular with many people, but in the end the scientific community reached the consensus that Allan was right. He performed a great public service by taking a courageous stand, especially since the Southwest Foundation provided the baboons used as organ donors and had the largest breeding colony of baboons in the world.

A selected list of Allan’s publications on this topic can be viewed at: http://xenotransplant.ineu.org/xenotrans/people/Allanj.htm.

Allan came to the Southwest Foundation as an assistant scientist in the Department of Virology and Immunology on June 15, 1987. He worked his way up through the ranks to become a scientist on December 26, 1992. He was involved in preparing the initial base grant application that led to the establishment of the Southwest National Primate Research Center (SNPRC) in 1999, and he served as leader of the SNPRC Retrovirus Diagnostics Laboratory until his death.

In addition to his role as a scientist at SFBR, Allan served as mayor of Helotes, Texas, from 2005 to 2007. Memorial donations may be made to: the Helotes Creek Nature Center, or the Helotes Humane Society.

SFBR Releases Fact Card of Accomplishments, Current Research Projects

The Southwest Foundation for Biomedical Research now provides a tool for its leaders and supporters to use in discussing the Foundation’s accomplishments and current work with the public, policymakers, members of the press, and others. The SFBR Fact Card is an easily portable list to keep on hand at all times.

During the summer of 2009, SFBR’s scientific and administrative leadership formulated a list of quick facts, specialized resources, accomplishments, and current research projects. The purpose of the document was to give SFBR leaders and others easily accessible information about the Foundation when talking to any audience interested in the organization’s work. SFBR makes the fact card accessible by printing a wallet-size card that can be carried in a wallet or purse to have on hand at all times. Included with this article is the list, which can be cut out and folded for carrying in wallets.

Foundation scientists and administrators who contributed to the development of the card include John L. VandeBerg, Ph.D., Jean L. Patterson, Ph.D., Sarah Williams-Blangero, Ph.D., Kenneth P. Trevett, Jeannie Frazier, Corbett Christie and Joseph Carey.
From Wine-Making to Unraveling a Disorder That Affects Millions of Pregnant Women

He nearly made a career in Australia’s booming wine industry. As a graduate student, Eric Moses, Ph.D., worked at a small winery as a biochemist, testing the grapes and wine and acting as the winemaker’s assistant. “I seriously considered becoming a winemaker and sometimes asked my housemate and closest friend to help me at the winery,” Moses said. His friend was so taken with this work that he left the university to study winemaking and is one of the most successful winemakers in Australia today.

But experiences provided by some very influential people drew Moses toward a path on which he has become a leading researcher of preeclampsia, a potentially fatal disorder that affects millions of pregnant women worldwide. (See sidebar page 5.)

A scientist in SFBR’s Department of Genetics, Moses, 54, has set out on a scientific quest to identify the genetic factors behind preeclampsia, with the hope of improving treatments and preventive therapies. Although there is no biochemical test for preeclampsia, it runs in families, a key element of his genetic studies.

Moses came to SFBR from Australia in early 2005 to focus on the genetic risk factors associated with preeclampsia. He works with an international group of collaborators zeroing in on those risk factors, as well as researching other pregnancy disorders.

Born in Sydney, Australia, Moses lived for his first five or six years in a small country town in northern New South Wales, where his father was a bank manager. Then they transferred to Melbourne. When he was young, he enjoyed tennis, swimming, surfing, fishing and camping.

His mother, a nurse, influenced his decision ultimately to pursue medical research. She talked about medical topics frequently while he was growing up, and by the age of nine, he knew that he wanted to go into medicine in some way. When he was 18, she arranged for him to get a summer job as an operating theatre orderly at Mercy Maternity Hospital in Melbourne.

He eventually took a position studying disorders of pregnancy with Professor Shaun Brennecke, an obstetrician at Melbourne’s Royal Women’s Hospital. “This man had a main research interest in preeclampsia,” Moses said. “It was meeting him and his commitment to making a difference in his field that inspired me.”

Prior to joining SFBR, Moses worked for 11 years at the Royal Women’s Hospital, where he became head of laboratory research for its Pregnancy Research Center. He continues to collaborate with Brennecke.

At SFBR, he started assembling a complementary team of people with different skills. “We knew that there was familial involvement, that preeclampsia runs in families,” he said.

Moses is investigating an area of the human genome on chromosome 2, which he mapped previously in a group of Australian families primarily recruited by Brennecke at the Royal Women’s Hospital. Moses’ group since then has also identified other suspect regions, known as “susceptibility loci,” on chromosomes 5 and 13.

With the help of SFBR’s AT&T Genomics Computing Center, and SOLAR, a software program developed by John Blangero, Ph.D., and his colleagues, Moses found the region on chromosome 2 that he believes contains a genetic variant involved with risk for preeclampsia, and later the regions on chromosomes 5 and 13.

In a separate study, Australian Matthew Johnson, Ph.D., a staff scientist in Moses’ group at SFBR, recently received a four-year American Heart Association fellowship to identify the specific genetic risk factors located on chromosome 5.

Much of Moses’ work aimed at identifying genetic risk factors for preeclampsia is supported by grant funding from the National Institutes of Health. His research also has been funded by the Southwest Foundation Forum.
What is Preeclampsia?

Preeclampsia is a treatable syndrome that strikes without warning and is marked by a sudden increase in a pregnant woman’s blood pressure after the 20th week of pregnancy. It has multiple symptoms, including high blood pressure, elevated protein in the urine, swelling of the face and hands, liver enzyme changes and other problems, such as headache, blurred vision or abdominal pain. Preeclampsia can affect the kidney, liver and brain.

The disorder affects three percent to five percent of pregnant women, according to the National Institutes of Health. In the United States, where treatments are available, few women die from preeclampsia. But, complications — such as kidney failure, hemorrhage, and stroke — from preeclampsia can lead to lasting health problems. In less industrialized nations, preeclampsia is one of the leading causes of maternal death, responsible for an estimated 75,000 deaths each year.

“When many things go wrong, a lot of the major organs are affected,” said Eric Moses, Ph.D., an SFBR geneticist who specializes in preeclampsia research. “When a woman is severely ill, delivery is the only way to alleviate the high blood pressure. If the condition is not stopped, it can lead to eclampsia. Eclampsia brings multiple organ failure and seizures that can lead to death.”

If preeclampsia develops, the only cure is delivering the fetus. The health care provider may develop a plan to try to prolong the pregnancy to give the fetus more time to grow and mature. At the same time, the health care provider will closely watch the health of the mother for signs that the fetus needs to be delivered right away, even prematurely, if necessary. If the preeclampsia is severe enough and the fetus is not delivered, the mother could die.

There is no proven way to prevent preeclampsia. But some women are more likely to develop it, including women who:
- Have high blood pressure before becoming pregnant.
- Are obese.
- Had high blood pressure or preeclampsia in previous pregnancies.
- Are younger than age 20 or older than age 40.
- Are pregnant with more than one baby.
- Have certain health conditions, such as diabetes or kidney disease.

Sources: Eric Moses, Ph.D., and the Eunice Kennedy Shriver National Institute of Child Health and Human Development

Moses’ collaborations include scientists in Australia, Ireland and Norway. “We’re building an international program to develop major studies on preeclampsia and to come up with answers related to major pregnancy problems,” Moses said. “We argue that what we will find is likely to be relevant to other later-life common disease outcomes.” And that they will make genetic discoveries that eventually will apply to women who are not pregnant, as well as to men.

Moses is married to Andrea Barrett, a native of Ireland, who specializes in executive coaching for top business executives and organizational leaders. They have two sons, Oscar, 9, and Leo, 7, whose Texas accents are amusing to their overseas relatives. Moses also has two older children, Ryan, 27, and Kate, 25, who both live and work in London, England.

Barrett and Moses enjoy the warmth and clear skies in San Antonio, and have been pleasantly surprised by the quality of the city’s arts scene. Early on weekend mornings, Moses is out on Hill Country roads riding his BMW sport touring motorcycle and dreams of taking a long motorcycle trip through the Western Mountain States.

And although he decided to forego the career in winemaking, Moses still has a passion for fine wine. And his close association with the field has influenced the successful food and wine-related career of son Ryan, who worked vacations at the Australian vineyard and winery of Moses’ old college buddy.

Can history repeat itself?

Among SFBR’s Many Accomplishments

- Developed high frequency ventilator to rescue premature babies from death or lifelong disabilities.
- Played key role in developing the current hepatitis B vaccine now administered in 116 countries.
- Identified genes that influence heart disease, diabetes, obesity, and other common health problems.
- Developed vaccines, antibodies and antitoxins for deadly agents of bioterrorism such as Ebola, botulinum neurotoxin, and anthrax.
- Developed promising hormone-derived therapies with potential to treat breast and prostate cancer.
- Developed invaluable animal models for research on cancer, heart disease, obesity, AIDS, and hepatitis among other public health problems that afflict millions around the globe.
- Created methods to diagnose infections with herpes B virus, which is lethal to humans.
- Discovered genes influencing drug resistance to malaria parasites.
- Verified efficacy of surfactant treatment to prevent or treat pulmonary distress in premature infants.

Clip and Save
Handy pocket-sized information sheet on SFBR’s work, resources and accomplishments.
Pemmaraju N. Rao, Pioneer in Women’s Health, Retires

The lifetime achievements of Pemmaraju N. Rao, Ph.D., an invaluable member of the SFBR community for 51 years, were acknowledged at a retirement celebration for him on September 14, 2009.

“His life is an outstanding example of the pioneer spirit,” said SFBR President Kenneth P. Trevett. “In 1958, he made an extraordinary decision, coming to San Antonio to work at the Southwest Foundation when this organization was still in its infancy and the city leaders were barely envisioning a biomedical enterprise here.”

Rao received his B.S. degree in chemistry at Andhra University in India before he was 20 years old and his Ph.D. degree from Calcutta University when he was just 25. The recipient of a Fulbright Travel Grant and Postdoctoral Fellowship, he journeyed to the University of Rochester to study steroid synthesis in 1954 and 1955. He returned to his native land for three years to serve as junior scientific officer for steroid research at the National Chemical Laboratory in Poona, India.

In 1958, Rao was invited to SFBR by Nicholas T. Werthessen, Ph.D., to work with Leonard Axelrod, Ph.D. His laboratory was in a renovated barn on Callaghan Road.

Rao soon became the leader of the Organic Chemistry Department. His work became well known beyond the perimeter of this organization and the boundaries of Texas. With more than 30 years of National Institutes of Health funding through research grants and contracts, he became a critical scientific partner in the development of contraceptive research, thus changing the face of women’s health care—and fundamentally altering the role of women in our society. His scholarship and technological leadership is also contributing to new medical approaches for certain forms of breast cancer, endometriosis and other serious afflictions. He has an extensive portfolio of intellectual property and his work and that of his colleagues have formed the basis of Evestra, a company spun off from the Foundation in 2008 through the entrepreneurial leadership of J.R. Hurd and John Kerr.

In recognition of his status as a highly-valued colleague, an internationally respected scientist, and a true change agent in the field of women’s health, SFBR is naming that portion of the Slick-Urschel Building which housed the Department of Organic Chemistry the Dr. Pemmaraju N. Rao Wing. The plaque signifying this naming will read:

The Dr. Pemmaraju N. Rao Wing

In grateful recognition of fifty-one years of his pioneering scientific endeavor and intellectual leadership at the Southwest Foundation for Biomedical Research, this laboratory wing is named for Pemmaraju N. Rao, Ph.D.

Dr. Rao’s extraordinary achievements in the field of hormone regulation and women’s health have had a profound impact throughout the world. His transformational studies have vastly improved understanding of reproduction and birth control and given rise to novel treatments for cancer and other afflictions.

Some of SFBR’s Current Research Projects

- Investigating genetic and dietary factors that have major roles in influencing susceptibility to cardiovascular disease, diabetes, and obesity.
- Evaluating novel approaches to curing hepatitis C, which infects three percent of the world’s population and is the leading cause of liver failure in the US.
- Genetically characterizing the parasites which cause malaria and schistosomiasis, with the common goal of developing more effective drugs and disease control strategies for these global health problems.
- Studying genetic determinants of susceptibility to Chagas disease and intestinal worm infections in order to come up with novel strategies for these diseases common in the developing world.
- Studying ways of preventing or treating diseases caused by respiratory syncytial virus (RSV), herpes simplex virus, and dengue virus.
**SFBR Science Update**

**Advances in Parasitic Diseases, Understanding the Nervous System**

SFBR scientists have for the first time constructed a genetic map of the parasite that causes schistosomiasis, a chronic worm infection that can damage internal organs and, in children, impair growth and cognitive development. Schistosome parasites are flatworms that infect more than 200 million people a year worldwide. Infection results in an estimated 200,000 deaths annually in sub-Saharan Africa alone, while 20 million suffer severe disease, according to the World Health Organization (WHO).

“A genetic map is the essential tool needed for finding the genes that are responsible for drug resistance and pathogenesis in this parasite,” said Timothy Anderson, Ph.D., of SFBR’s Department of Genetics. “First, identification of mutations allows us to better understand the mechanism of action of the drugs used, and to redesign drugs to restore treatment efficacy. Second, identification of mutations involved allows us to efficiently monitor the spread of resistance in parasite populations using simple molecular methods.”

The new study was published in the June 30, 2009 issue of the journal *Genome Biology*, and was supported by the National Institutes of Health (NIH). Anderson’s initial work was funded by the Southwest Foundation Forum.

Anderson and his colleagues used two adult flatworms to breed 88 *S. mansoni* offspring. By comparing the genetic information of the offspring to the parents, they generated a genetic map of chromosomes of the pathogen. The scientists are planning further research using the genetic map to understand why some parasites cause more disease than others.

**Dengue Fever Clues**

In another new report, scientists have found in mice clues to why some strains of the dengue fever virus produce more severe disease than others, an important step toward developing a vaccine against the most deadly types.

“The results point to the Southeast Asian virus as the most virulent and the one that should be prioritized for elimination or control,” said SFBR virologist Rebeca Rico-Hesse, Ph.D., senior author on a new study appearing in the *Journal of Virology*. The research was supported by The Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation and the NIH.

Dengue viruses, which cause dengue fever and its more severe form, dengue hemorrhagic fever, in humans, have been spreading to more areas of the world along with their mosquito carriers. Now over 100 countries are affected, including the United States, where dengue is emerging as a public health problem in Texas and Hawaii.

Some 2.5 billion people — two fifths of the world’s population — are at risk from dengue, according to the WHO, which estimates there may be 50 million dengue infections worldwide every year.

In the new study, Rico-Hesse and her colleague Javier Mota, Ph.D., found that different genetic variants of dengue virus cause different clinical signs in mice reconstituted with human immune system cells. The Southeast Asian genetic variants of virus produced higher levels of the virus and rash in infected mice compared with American, Indian and West African types of virus.

Studies have begun to examine how lab-infected mosquitoes transmit the virus by bite to the mice, rather than by injection, to mimic the natural cycle of disease and to measure how many bites it takes to get disease. Vaccines or antivirals could then be developed.

**Repairing the Damaged Spinal Cord**

In other work, SFBR scientists are developing and expanding new collaborations in the fields of spinal injury and brain development with colleagues around the world.

This project is aimed at better understanding repair of the spinal cord following injury when it occurs at very early stages of development. It is based on the observation made by scientists at the University of Melbourne that damaged spinal cords of the opossum *Monodelphis domestica*, which are up to one to two weeks-old, have a remarkable ability to heal. This self-healing capability is completely lost by the age of four weeks. Investigators recently found that the greater healing ability of the seven-day-old opossums compared with older animals is associated with differences in the expression of genes involved in the inflammatory response to injury.

This collaboration is being expanded during 2009 and 2010 with the Australian group spending four weeks at SFBR this fall conducting experiments in which the spinal cords of young opossums are damaged at different postnatal ages and then studied for their ability to repair. This research is funded by The Kleberg Foundation, Australia’s Victorian Neurotrauma Initiative, and The Miami Project to Cure Paralysis.
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Editor: Joseph Carey, Vice President for Public Affairs
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