science building



TEXAS BIOMEDICAL RESEARCH INSTITUTE

2011 ANNUAL REPORT

Science



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FRONT, INSIDE COVER: This image shows smooth muscle cells derived from baboon embryonic stem cells. Alpha-actin-2, a cytoplasmic protein that is specific to smooth muscle cells, is stained green. The cell nuclei are stained blue.

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TEXAS BIOMEDICAL RESEARCH INSTITUTE

Enhancing lives through discovery"

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EXTRAORDINARY RESOURCES



BSL-4 LABORATORY

Texas Biomed maintains the only privately owned Biosafety Level 4 Laboratory in the United States



PRIMATE RESEARCH CENTER

The Southwest National Primate Research Center is an invaluable resource for developing animal models of human diseases



AT&T GENOMICS COMPUTING CENTER

Texas Biomed's AT&T Genomics Computing Center uses the world's largest computing cluster dedicated to human genetic analysis



HUMAN POPULATION STUDIES

Long-term human population studies examine the genetic basis of disorders such as heart disease, obesity and diabetes

ABOUT TEXAS BIOMED

AS ONE OF THE WORLD'S LEADING INDEPENDENT BIOMEDICAL RESEARCH INSTITU-TIONS, THE TEXAS BIOMEDICAL RESEARCH INSTITUTE IS DEDICATED TO ADVANCING THE HEALTH OF OUR GLOBAL COMMUNITY THROUGH INNOVATIVE BIOMEDICAL RESEARCH. TODAY, TEXAS BIOMED'S MULTIDISCIPLINARY TEAM OF 73 DOCTORAL-LEVEL SCIENTISTS WORKS ON MORE THAN 200 MAJOR RESEARCH PROJECTS.

Located on a 200-acre campus in San Antonio, Texas, the Institute partners with hundreds of researchers and institutions around the world, pursuing advances in the prevention and treatment of heart disease, diabetes, obesity, cancer, osteoporosis, psychiatric disorders, tuberculosis, AIDS, hepatitis, malaria, parasitic infections, and a host of other diseases.

Texas Biomed is the site of the Southwest National Primate Research Center, which houses the world's largest research colony of baboons, including a unique pedigreed group that is invaluable for genetic studies on complex diseases. The Institute enjoys a distinguished history in the innovative, humane, and appropriate use of nonhuman primates in biomedical research.

The Institute 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 laboratory designed for maximum containment, Texas Biomed investigators can safely study deadly pathogens for which there currently are no treatments or vaccines.

Institute scientists also built the world's largest computing cluster for human genetic and genomic analysis. Housed in the AT&T Genomics Computing Center, the parallel-processing network allows Texas Biomed geneticists to search for diseaseinfluencing genes at record speed. Texas Biomed's population studies include the genetics of complex diseases in a variety of people, including Mexican Americans, American Indians, Alaskan Natives, and Middle Easterners. A project in Nepal, for example, is looking at the genetic components of susceptibility to intestinal worm infections using newly developed statistical genetic methods.

Created through the philanthropic vision of Thomas B. Slick Jr. in 1941 and known until recently as the Southwest Foundation for Biomedical Research, Texas Biomed relies on philanthropy to enhance its capabilities. Approximately 75 percent of the Institute's annual budget is funded by highly competitive, peerreviewed federal research grants and contracts, while another 3 percent comes from commercial contracts with biotechnology and pharmaceutical firms. Philanthropy constitutes the secondlargest portion of the Institute's budget: More than one-fifth of Texas Biomed's expenses are met by the generous contributions of foundations, corporations, and individuals, as well as income from Texas Biomed's endowment and royalties.

For more information on the Texas Biomedical Research Institute and its efforts to improve human health, contact the Institute at 210-258-9400, or visit our Web site at www. TxBiomed.org.

W W W.T X B I O M E D. O R G



Enhancing lives through discovery"

LETTER FROM THE PRESIDENT



PURSUING THE FULFILLMENT OF OUR MISSION—THAT IS, TO IMPROVE THE HEALTH OF OUR GLOBAL COMMUNITY THROUGH INNOVATIVE BIOMEDICAL RESEARCH—IS A **RESPONSIBILITY**, NOT JUST A JOB. EVERYONE FEELS IT AT TEXAS BIOMED, AND EVERYONE KNOWS THAT SINCE WE CAN MAKE A DIFFERENCE, WE **SHOULD** MAKE A DIFFERENCE ... A BIG DIFFERENCE.

> And that is why we have an ambitious agenda of new construction, recruitment of additional scientists, individual and collaborative efforts to address the most pernicious and deadliest diseases, and a new name to help put a public face on what we do.

Seventy years ago, our founder, Tom Slick, envisioned a research organization in San Antonio that would contribute to improved health throughout the world. What an audacious dream in a city where there was no medical school and no graduate programs in the biomedical sciences! What he started and what is continuing today is a multifaceted, world renowned organization where discoveries in genetics and virology, as well as the development of primate models of human diseases, are laying the foundation for better treatments and cures for hepatitis, diabetes, obesity, heart and circulatory illness, mental disorders, AIDS, spinal cord injury, and cancer. Furthermore, we are exploring new vaccine strategies to protect whole populations from the ravages of infectious pandemics as well as the brazen and irresponsible attacks of bioterrorists.

Texas Biomed is also participating in several collaborative and interdisciplinary efforts with other institutions in the city to facilitate vaccine development, stem cell approaches to tissue repair, musculoskeletal research to address arthritis and osteoporosis, new diagnostic and treatment strategies against type 1 and 2 diabetes, and tumor genomic analysis that can lead to more personalized approaches to cancer. What Tom Slick envisioned has come to pass. What you envision—a healthier future for your family and friends—will come to pass with your continued goodwill, support, and counsel. As this report goes to press, the generosity of this community is enabling us to start construction on a 70,000 square-foot building complex with 15 new laboratories—a significant step toward giving us greater capacity to facilitate discovery. This new building will allow Texas Biomed to retain and attract the world-class talent and research programs that will guide advances made here well into mid-century.

Thank you so much for your continued interest in our work. We will strive every day to merit your expectations and your trust.

KENNETH P. TREVETT, J.D., PRESIDENT AND CEO

"WHAT TOM SLICK ENVISIONED HAS COME TO PASS. WHAT YOU ENVISION — a bealthier future for your family and friends — WILL COME TO PASS WITH YOUR CONTINUED GOODWILL, SUPPORT, AND COUNSEL."

KENNETH P. TREVETT,
 PRESIDENT AND CEO

TEXAS BIOMEDICA TEXAS BIOMEDICA

LETTER FROM THE CHIEF SCIENTIFIC OFFICER



SCIENTISTS AT THE TEXAS BIOMEDICAL RESEARCH INSTITUTE HAD AN OUTSTANDING YEAR IN 2011 DURING WHICH THEY MADE MAJOR ADVANCES THAT CONTRIBUTED TO THE INSTITUTION'S MISSION OF IMPROVING THE HEALTH OF OUR GLOBAL COMMUNITY AND ENHANCING LIVES THROUGH DISCOVERY.

During 2011, Texas Biomed investigators published well over 100 manuscripts in the national and international scientific literature. Each one is a step toward fulfilling our quest to understand human biology and to develop new strategies to protect humanity from the scourges of devastating illnesses. These advances include:

- Demonstration with baboons that even a moderate reduction in maternal nutrition during pregnancy has a detrimental impact on brain development of the fetus (Proceedings of the National Academy of Sciences U.S.A. 108:3011–3016, 2011). This result implies that the brain function of children whose mothers had suboptimal nutrition during pregnancy may be altered throughout their lives.
- Establishment of a nonhuman primate model (the common marmoset) that mimics the human disease process of Ebola and other hemorrhagic fevers (*Human Vaccines* 7:667–673, 2011). This new model paves the way for testing vaccines that can prevent

these deadly diseases during natural outbreaks in Africa or as a consequence of terrorist acts.

- Advancement of our understanding from research with chimpanzees of the mechanisms by which all individuals are able to clear the hepatitis A virus, whereas many are not able to clear the hepatitis C virus (*Proceedings of the National Academy* of Sciences U.S.A. 108:11223–11228, 2011). The results of this study may contribute to the design of vaccines and drugs for the prevention and treatment of hepatitis C.
- Identification in humans of a new gene whose expression level negatively correlates with a risk of major depression in Mexican Americans (*Biological Psychiatry* 71:6–14, 2011). This gene is a novel drug target for pharmacotherapeutics designed to treat major depression disorders.

During 2011, Texas Biomed scientists were awarded \$32 million in grant and contract funding. Six new multiyear grants in excess of \$2.3 million were awarded. This level of success in the current difficult funding environment attests to the high level of creativity and competitiveness of our scientists.

Although federal and contract support is important, the interest, enthusiasm, and generosity of our Board of Trustees and the rest of the San Antonio philanthropic community also is crucial. It enables Texas Biomed investigators to conduct small, innovative research projects that will eventually result in much larger grants that support new research programs.

Looking ahead to the future and the anticipated completion in 2013 of a new 70,000 square-foot building for 15 new laboratories and new programs, the Texas Biomedical Research Institute will markedly strengthen its capacity to conduct lifesaving research and to improve lives worldwide.

Sincerely,

John I Vande Berg

JOHN L. VANDEBERG, PH.D., CHIEF SCIENTIFIC OFFICER

"SIX NEW MULTIYEAR GRANTS IN EXCESS OF \$2.3 MILLION WERE AWARDED. THIS LEVEL OF SUCCESS IN THE CURRENT DIFFICULT FUNDING ENVIRONMENT ATTESTS TO *the high level of creativity and competitiveness of our scientists.*"

> - JOHN L. VANDEBERG, PH.D., CHIEF SCIENTIFIC OFFICER

ENHANCING CAPACITY

Increasing Research Capacity to Advance Science, Enhance Health

DURING 2011, A WIDE MOUND OF DIRT WAS DEPOSITED ON THE NORTH SIDE OF THE TEXAS BIOMED CAMPUS NOT FAR FROM THE MILITARY DRIVE GUARD HOUSE. ALTHOUGH ITS APPEARANCE LEAVES SOMETHING TO BE DESIRED, BY 2013 IT IS SCHEDULED TO BE THE SITE OF A NEW LABORATORY COMPLEX THAT WILL VASTLY EXPAND RESEARCH CAPACITY AND TRANSFORM THE LOOK OF THE CAMPUS.

The proposed 70,000 square-foot building will provide much needed laboratory and administrative space for the Southwest National Primate Research Center (SNPRC). The building will also add laboratory and administrative space for the Department of Virology and Immunology, as well as executive administrative office space.

Texas Biomed's Board of Trustees approved the enhancement plan and selection of architectural firms in 2010 and 2011 respectively. The building is part of a campus master plan that includes a major effort to recruit world-class scientists, enhance existing research programs, and initiate new ones to accelerate the pace of discovery.

"A transformational expansion of the Texas Biomed campus will soon become a reality," said Texas Biomed Board Chair J.R. Hurd. "Thanks to the work of our architects—Lake Flato and FKP Architects—our new laboratory and office buildings will make a compelling statement about the vision and energy of our institution." Chief Scientific Officer John L. VandeBerg, Ph.D., added: "The new laboratories will greatly enhance our capacity for discoveries that advance science and medicine, while the relocation of our support service departments and administrative units into key adjacencies will significantly increase

efficiency. Seeing this vision, which we have been developing for more than a decade, being transformed into reality is one of the most exciting institutional accomplishments that I have witnessed over my more than 30 years at Texas Biomed."

NEW RESEARCH PROGRAMS

Elements of the strategy include recruiting six additional faculty members in the Genetics and Virology and Immunology departments. A new director and a junior faculty member also will be recruited for the SNPRC. The goal of these recruitments will be to promote the translation of discoveries into medical applications. Texas Biomed also plans to develop a regenerative medicine program to advance the effort to replace dead or dying tissue in people with a variety of conditions and illnesses. This effort, which will involve recruiting two additional researchers, will include collaborations with other investigators in San Antonio.

The new \$25 million building will provide an attractive "front door" for Texas Biomed and represent the public face of the campus. "For the first time in its 70-year history, our institution will have a building with the organization's name that clearly identifies who we are," said Texas Biomed President Kenneth P. Trevett. "The building will represent a powerful symbol of the forward thinking of our founder, Tom Slick, our trustees, and staff.

"With more scientific personnel and improved facilities, we will make even greater contributions to addressing deadly and lifealtering diseases. That's our mission, and that's our goal," he added.

FIFTEEN NEW LABORATORIES

The laboratory and office building will consist of 15 research laboratories, shared instrument rooms for these laboratories, and equipment and service space. The complex also will consolidate researchers and laboratories now housed in multiple buildings around the campus and will substantially increase efficiency of research through shared staff and equipment. The building will provide space for a number of nationally prominent visiting scientists who will collaborate with Texas Biomed researchers. And it will serve as a visible focal point for the SNPRC, one of only eight such centers in the United States and the only one in the Southwest.

A NEW CAMPUS FRONT DOOR

"Texas Biomed challenged the design team to create a transformative project that would be the new front door and public face of the campus. Since this is a research facility, this building also needs to be technically highfunctioning and must represent good cost value to the Institute," said Tom Woods, vice president of FKP Architects in Houston, a firm that specializes in laboratory design.

"Biosafety labs are always a challenge and require a lot of attention to detail during design and construction because they must meet the very stringent requirements of the Centers for Disease Control," he added.

The design of the new headquarters honors the Slick legacy and adds a new level of detail and artistry to the campus with its use of tilt-wall construction for the new building's facades.

"The concrete structures with etched glass in the lobby areas and treated window glazing to reduce solar glare modernize the campus and elevate the existing buildings while relating to them. These structures also are pragmatic and economical," said Greg Papay of Lake Flato Architects in San Antonio, the firm charged with designing the overall look of the new buildings. "WITH MORE SCIENTIFIC PERSONNEL AND IMPROVED FACILITIES, WE WILL MAKE *even greater contributions to addressing deadly and life-altering diseases*. THAT'S OUR MISSION, AND THAT'S OUR GOAL"

- KENNETH P. TREVETT

Thinner in profile than many of the existing campus buildings, the new buildings allow natural light to diffuse into the office and lab areas and afford views out to the new landscaped "front yard" and lushly planted courtyard that will stitch the new building into the rest of the Texas Biomed campus. The building's shape, orientation, and systems also work together integrally to reduce overall energy use. Current projections show that the new structure will operate at 20 percent better efficiency than current building codes require, Papay said. This energy efficiency, combined with other environmentally appropriate decisions with respect to the site design, water consumption, building materials, and indoor environmental quality, has the project tracking to achieve certification from the U.S. Green Building Council's Leadership in Energy and Environmental Design rating system.

Overall, the new facility will be important to donors and staff and will be an exciting mechanism for retention and recruitment of world-class scientists. Among the major goals are to replace aging SNPRC facilities; provide a comfortable, attractive facility for Texas Biomed and visiting scientists; bring together administrative offices and laboratories that are currently spread across the campus; and create a building with a bold design that is in keeping with current campus materials and aesthetics while making the best use of the Institute's finances.

For the 70,000 square-foot building, bidding and construction is scheduled to commence in early 2012 with completion projected within 18 months.

MASTER PLAN

The campus master plan also envisions projects that will address needs far into the future—as much as 25 years—which is a significant planning horizon, considering the blistering pace of innovation in science. The plan includes support infrastructure engineering, energy, utilities, communications, and transportation—and provides more open, green, and pedestrian-friendly spaces. This plan also will involve a rearrangement of the campus with a new entrance and new courtyard and common areas that will make Texas Biomed a more aesthetically pleasing place to work and visit.

And make that mound of dirt a distant memory.

6

additional faculty members in the Genetics and Virology and Immunology departments

2

additional faculty members recruited for the SNPRC

2

additional researchers recruited for a regenerative medicine program

70k

square footage of new laboratories and scientific service space

15

additional research laboratories

24

additional units of animal rooms

CAMPAIGN REPORT

ENHANCING THE VISION

Scientific entrepreneurship has been a hallmark of Texas Biomed from its founding in 1941. Because of the "Enhancing the Vision" Campaign, Texas Biomed researchers will be able to maintain this highly productive tradition and tackle the world's most difficult medical challenges.

Led by Chair J.R. Hurd and Campaign Co-Chairs John Kerr and Ron Calgaard, the trustees have personally pledged more than \$16.5 million and another \$8.2 million from their companies and foundations during the Campaign's "Quiet Phase." By press time, more than \$30.5 million has been raised altogether for faculty recruitment and construction of the 70,000 square foot laboratory complex. Lead donors to the Campaign are recognized below and in the Roll of Donors on page 41 of this report.

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For a complete list of all donors to date, please turn to page 41.



SNPRC ROUNDTABLE

ESEARCH AT TEXAS BIOMED'S SOUTHWEST NATIONAL PRIMATE RESEARCH CENTER (SNPRC) OFFERS GREAT PROMISE FOR UNDERSTANDING AND TREATING INFECTIOUS DISEASES AND IDENTIFYING THE GENETIC COMPONENTS OF SUSCEPTIBILITY TO COMMON DISEASES OF PUBLIC HEALTH IMPORTANCE. MUCH OF THIS WORK IS AIDED BY THE SNPRC'S PEDIGREED BABOONS AND COLONIES OF CHIMPANZEES, RHESUS MONKEYS, AND OTHER SPECIES. FOR THIS ROUNDTABLE DISCUSSION, ANNUAL **REPORT EDITOR JOSEPH CAREY** INTERVIEWED FOUR TEXAS BIOMED SCIENTISTS CLOSELY INVOLVED IN SNPRC RESEARCH.

THE SCIENTISTS ARE (LEFT TO RIGHT): ROBERT E. LANFORD, PH.D., IN THE DEPARTMENT OF VIROLOGY AND IMMUNOLOGY; THOMAS FOLKS, PH.D., SNPRC'S ASSOCIATE DIRECTOR FOR RESEARCH RESOURCES; AND LORENA M. HAVILL, PH.D., AND ANTHONY COMUZZIE, PH.D., IN THE DEPARTMENT OF GENETICS.

SNPRC ROUNDTABLE

DURING THE LAST 10 YEARS, WE HAVE FOCUSED ON TESTING NEW THERAPIES FOR HEPATITIS C THAT HAVE **BEEN DEVELOPED BY** PHARMACEUTICAL COMPANIES. This has led drugs given together SOME OF WHICH HAVE **BEEN TESTED HERE.**"

- ROBERT LANFORD, PH.[

Q: Dr. Lanford, you have been involved in primate center-related research projects for the 28 years that you have been at Texas Biomed. Please describe your current focus of research, important findings, and where you see it headed in the near future.

ROBERT LANFORD: Today hepatitis C virus (HCV) infection, which is chronic in about 4 million Americans, is the number one cause of liver transplantation and the most rapidly increasing cause of death from liver cancer in the United States. During the last 10 years, we have focused on testing new therapies for hepatitis C that have been developed by pharmaceutical companies. This has led to the development of antiviral cocktails, multiple different drugs given together to cure hepatitis C, some of which have been tested here. With hepatitis C, we knew we would eventually come up with a cure, and that occurred in 2011, much sooner than we thought. A number of companies now have cocktails in clinical trials that cure most HCV infections in less than 12 weeks without using the really harsh therapy known as interferon. This breakthrough is due to the efforts of the scientific community and animal models, such as the chimpanzee.

The next thing is to develop a vaccine, and some are going into human trials right now. If we are fortunate, some of those vaccines will be effective. Several of them have already been tested in chimpanzees and have shown some promise, but there are still failures. We really don't have good markers for what goes wrong when the immune system fails and why it fails. Some immune and gene expression technologies are allowing us to probe further into that.



In one of our new programs just funded by the National Institutes of Health (NIH), we are using something called antisense technology to knock down the expression of specific genes involved in the innate immune response of the marmoset to determine which genes are critical for preventing chronic infections. This is the first time gene knockdown has been performed in a systematic manner in a primate. If successful, we believe this model can be used to study other diseases and to identify specific genes that may be therapeutic targets.

Q: What are some of the other research programs in the department?

ROBERT LANFORD: Ricardo Carrion and Jean Patterson have developed the marmoset as a model for infection with the Ebola and Marburg viruses, which cause hemorrhagic fever. Robert Davey is using viral-like proteins to understand the cellular pathways that are required for infection by these hemorrhagic fever viruses and is screening small molecules to block these infections. (See article on biodefense, page 24.) Both Marie-Claire Gauduin and Luis Giavedoni work on simian immunodeficiency virus (SIV), the primate model of HIV infection. Their strategy is to make SIV vaccines that work in animals and then recast them to work as HIV vaccines in humans.

Q: Any idea when some of these vaccines may get to the FDA for approval?

THOMAS FOLKS: Probably not until the latter part of this decade. More and more work is going to be needed in the monkey model because testing in enough humans to get reliable results is going to be very hard to afford. So, you are really relying on the animal model to be your first attempt to see if a vaccine is efficacious.

ANTHONY COMUZZIE: It's always important to reiterate that biology is messy, and yet this naïve opinion is out there that you can replace a whole organism with some sort of statistical model or cells in a petri dish. They can never replace the complexity of a living organism.

Q: Dr. Comuzzie, you are working on obesity and diabetes. Please describe your major focus on these disorders.

ANTHONY COMUZZIE: In my 20 years here, we have seen that cardiovascular disease, obesity, diabetes, and hypertension are all incredibly

interrelated. So you can't really do work on one of these conditions without having to be cognizant of work with some of the others. I evenly split my efforts between nonhuman primates and human populations, and this allows me to work in a translational paradigm. For example, with the things we find in human genes, we can go back and look at nonhuman primate models. Or we can control aspects of the environment of the baboon that we can't control in humans.

In the last decade, we have increased our study of physiology because it's very difficult to focus just on the genetics when we really don't understand all the physiology. One of the things we are trying to do in parallel between our human studies and nonhuman primate studies is to map genes that regulate susceptibility. These conditions are complex, and they are not simply genetic in origin. There are also very important environmental triggers, such as diet.

You can't change a person's genetics, but you may be able to modify aspects of the environment or, perhaps even more importantly, manipulate the environment along with understanding the genetic underpinning so that you can get the most effective types of treatment.

During the last five years, we have begun to think about the modern American diet as not just high in fat, but also high in simple carbohydrates. There is growing evidence that while fat may be a component of the diet that induces the damage to vasculature and leads to these other metabolic disruptions, it's not sufficient in itself to do that. For our nonhuman primate studies, we have developed a diet that's more in keeping with the nutritional composition of the typical American diet by adding in simple carbohydrates. This is allowing us to identify additional genetic pathways involved in the metabolism of both fat and carbs, and even the sort of synergistic interaction between the carbs and fat in the diet.

Q: Dr. Havill, please tell us about the value of the baboon colony in your research on osteoporosis and osteoarthritis.

LORENA HAVILL: I came to San Antonio 10 years ago because of the value I saw in the baboon for studying two age-related diseases of the bones and joints: osteoporosis and osteoarthritis. Simply put, to get good answers about how these diseases start and progress, we need to study animals that develop them naturally the way humans do. Other readily available animal models (mice and rats) just aren't susceptible to these age-related skeletal disorders.

Q: Please describe some of your current projects, results, and what you see happening over the next few years.

LORENA HAVILL: In osteoporosis, my collaborators and I are working on ways to get a better picture of what puts some people at higher risk for breaking a bone. This work, funded by the NIH, could revolutionize the way we view bone strength. Doctors evaluate your risk of breaking a bone by doing a bone scan to see how dense your bones are. Current medical thinking is that the denser the bone, the less likely it is to break. The problem is that roughly half of the people who break a bone actually pass the bone density test. I am working with engineers at the Southwest Research Institute to identify other factorsarrangement of bone tissue, mineral and chemical properties, for example—

"THIS NAÏVE OPINION IS OUT THERE THAT YOU CAN REPLACE A WHOLE ORGANISM WITH SOME SORT OF STATISTICAL MODEL OR CELLS IN A PETRI DISH They can never replace the complexity of a living organism."

– ANTHONY COMUZZIE, PH.E

"THE BABOON BONES THAT I'VE COLLECTED OVER THE PAST DECADE GIVE US THE *opportunity*, FOR THE FIRST TIME, TO REALLY LEARN ABOUT THE EARLY STAGES OF OA, BEFORE IT IS DETECTABLE ON X-RAY."

– LORENA M. HAVILL, PH.D.

SNPRC Roundtable (continued)

that explain the fracture risk in the other 50 percent so that doctors can begin including these other measurements in their testing. Osteoarthritis (OA) is especially interesting because for years it has been viewed as a natural consequence of using your joints: "wear and tear." Now we know that it's not that simple. There are marathon runners and elderly people who are arthritis-free. What protects these individuals when other people are developing arthritis at age 30? And how does the disease start?

We know that eventually you get cartilage damage and you get bone build-up, but we know virtually nothing about the changes in joints that are happening in the earliest stages. The baboon bones that I've collected over the past decade give us the opportunity, for the first time, to really learn about the early stages of OA, before it is detectable on X-ray. My collaborators and I are comparing the genetic makeup of baboons with early OA, as compared with those with healthy joints, to see what differs between the two. We are also comparing the genetic makeup of elderly baboons with OA against those who seem to be protected from the disease. The ultimate goal is to identify biological mechanisms that are responsible for OA development and progression and for maintaining healthy joints as we age.

> Microscopic view of bone formation in the baboon.



Q: Dr. Folks, please tell us about some of the changes occurring at the primate center.

THOMAS FOLKS: You have just heard about some of the great science going on right now, but you have to remember that the primate center has been here for 50 years and that it has been serving our internal scientists for a long time. About 13 years ago, it became a national primate research center, which is one of eight in the nation, and with that came the obligation to involve more outside people and services. The outside work ranges across all of the species, and even though we will probably slow down somewhat in chimpanzee research, we have increased outside interest in work with other species.

Q: Dr. Folks, does the SNPRC get certain types of requests from outside investigators more than others?

THOMAS FOLKS: It goes back and forth, depending on the interests of federal

funding agencies. A group in Indianapolis, for instance, is very interested in transplants of pig livers to baboons as bridging agents for xenotransplantation. Others are considering the primate center for studies of aging. The marmoset, because of its short longevity, is an excellent animal for research on aging. One investigator is looking at the effects of nutrition on aging in the marmoset. Others are looking at the baboon for changes in the immune system. The SNPRC also has a very mature biomaterials service to provide tissues to researchers.

Q: There are plans to move some primate center scientists to the new building, which is part of the campus expansion. How will that affect what you do, and does it present new opportunities?

THOMAS FOLKS: We are excited about it. Dr. Lanford's laboratory will be going into the new building, and the Immunology Core Laboratory When we became a national primate research center, with that came the obligation to involve more outside people and services ranging across all species.

will also move to the new building along with a very new and sophisticated biosafety level 3 flow cytometry facility. This is going to help with a lot of the work we do in HIV and SIV.

Q: What will be the impact of the recent Institute of Medicine (IOM) report limiting chimpanzee research and the NIH response?

ROBERT LANFORD: The three criteria used by the IOM committee to justify chimpanzee research are the same criteria we've always used. The recent report has accelerated something that was in the plan anyway.

It is premature to limit chimpanzee research, however. Today we do not yet have an HCV vaccine, and there are some things on the horizon that involve chimpanzees — such as studying the very complex process of altering the immune response in people that have autoimmune diseases that cause type I diabetes and rheumatoid arthritis.

ANTHONY COMUZZIE: A two-edged sword is in play. One of them is you don't want to use an animal model that is more than you need. If a rodent really will work, then you should work with a rodent. At the same time, if rodents, dogs, or any other animals are not going to give you a viable usable answer, you shouldn't use them. If you can do it without using chimpanzees, that's a good thing. Yet there is a very real political agenda coming from individuals whose ultimate goal is to stop animal-based biomedical research. So it is important to us as a community of investigators to make the public aware of the fact that we understand and appreciate this issue and that we use chimpanzees only because there is real value to be gained.

THOMAS FOLKS: A moratorium on chimpanzees in biomedical research was not recommended by the IOM committee. The chimpanzee is still available for tests where it is the only animal we could use. But the bigger question now is whether attempts will be made to limit research with other species.

Q: Looking to the future, are there any areas of research where the primate center could expand to maintain its viability?

ROBERT LANFORD: We need to develop more biologics, drugs, and vaccines made from living organisms. We have tested biologics in chimpanzees to see whether or not they are having the intended function. The argument for using other species is valid, and so we can now engineer all of these biologics so that they have the same reactivity in a baboon or macaque monkey as they do in humans. There is also a big opportunity in small molecules that is going to impinge on these very complex diseases. **THOMAS FOLKS:** The whole translational research concept will increasingly involve regeneration, personalized medicine, progenitor cell studies, and stem cells. We are looking to develop programs in these areas during the next five years.

ANTHONY COMUZZIE: The only way personalized medicine is going to be developed is by having an individual completely characterized genetically, and you have to have a good medical history to be able to determine where you are and where you're trying to go. The fact that we have these deep pedigrees with the baboons, going back eight generations, is very important. With the whole baboon sequence shortly to be available, we've got a place to field-test the whole concept in a way that we couldn't effectively do in humans.

THOMAS FOLKS: Medicine is going in a lot of different directions, and the effect of environmental factors on the genetics of disease is going to be very important. It's like you have a ramp on the table here and you put a marble on it, and let it roll off. Do it more than once, and the marble rolls off differently each time. Why is that? Genetics is exactly the same. And that's one reason why we've got so much more work to do. "MEDICINE IS GOING IN A LOT OF DIFFERENT DIRECTIONS, AND THE EFFECT OF ENVIRONMENTAL FACTORS ON THE GENETICS OF DISEASE *is going to be very important.*"

HOMAS FOLKS, PH.D.



2011 DISCOVERIES:

Restrictive Diet During Pregnancy Predisposes to Impaired Brain Development, Diabetes

EPARATE STUDIES IN BABOONS BY TEXAS BIOMED SCIENTISTS UNDERSCORE THE IMPORTANCE OF A MOTHER'S DIET ON THE CHANCES HER OFFSPRING WILL HAVE IMPAIRED BRAIN DEVELOPMENT AND RISK

FOR DIABETES LATER IN LIFE.



"OUR COLLABORATION ALLOWED US TO DETERMINE THAT A MODERATE REDUCTION IN THE NUTRITIONAL ENVIRONMENT *impacts the fetal brain* AT BOTH THE CELLULAR AND MOLECULAR LEVELS."

— LAURA COX, PH.D.

The studies point to the importance of the environment in addition to genetic factors influencing early development and health as people age. They also illustrate how one factor can influence several conditions at a time.

In one study, the research team reported that inadequate nutrition during early pregnancy impairs fetal brain development. Utilizing

baboons in Texas Biomed's Southwest National Primate Research Center, the researchers found decreased formation of cell-to-cell connections, cell division and amounts of growth factors in the fetuses of mothers fed a moderately reduced diet during the first half of pregnancy.

The study, published in *Proceedings of the National Academy of Sciences USA*, and funded by the National Institutes of Health and the German Federal Ministry of Education and Research, also included scientists from the University of Texas Health Science Center at San Antonio (UTHSCSA) and Friedrich Schiller University in Jena, Germany.

NUTRITIONAL ENVIRONMENT

"Our collaboration allowed us to determine that a moderate reduction in the nutritional environment impacts the fetal brain at both the cellular and molecular levels," said Texas Biomed's Laura Cox, Ph.D. "That is, we found dysregulation of hundreds of genes, many of which are known to be key regulators in cell growth and development, indicating that nutrition plays a major role during fetal development by regulating the basic cellular machinery."

The team compared two groups of baboon mothers, one eating as much as they wanted during the first half of pregnancy and the other receiving 30 percent less food, a level of nutrition similar to what many prospective mothers in the United States experience. The baboon's brain developmental stages are very close to those of human fetuses, the researchers noted. Most previous research in this area was conducted in rats.

"This study is a further demonstration of the importance of good maternal health and diet," said senior author Thomas McDonald, Ph.D.,

THE VALUE OF DIET

Utilizing baboons at Texas Biomed's SNPRC, researchers found decreased thickness of fetuses' frontal cortex from mothers fed a moderately reduced diet during the first half of pregnancy (a level of nutrition similar to what many prospective mothers in the U.S. experience) compared to those fed as much as they wanted.

BABOONS FED NORMAL DIET



of UTHSCSA. "It supports the view that poor diets in pregnancy can alter development of fetal organs, in this case the brain, in ways that will have lifetime effects on offspring, potentially lowering I.Q. and predisposing to behavioral problems."

It is known that marked nutrient restriction, such as in famine conditions, adversely affects development of the fetal brain. But McDonald said this study "is the first demonstration of major effects caused by the levels of food insecurity that occur in sections of U.S. society and demonstrates the vulnerability of the fetus to moderate reduction in nutrients."

Researchers now must review the commonly held notion that during pregnancy the mother is able to protect the fetus from dietary challenges such as poor nutrition, he said.

TYPE 2 DIABETES IN THE WOMB

In a second study, Texas Biomed scientists reported that inadequate nutrition during pregnancy predisposes offspring to becoming prediabetic before adolescence.

> The study, conducted in 18 baboons, found that when mothers are even moderately undernourished while pregnant and breastfeeding, their offspring are consistently found to be prediabetic before adolescence.



from the nutritionally restricted mothers showed increases in fasting glucose, fasting insulin and other hallmarks of prediabetes – the other twelve did not.

A CRITICAL TIME

"This is a critical time window when many of the neurons as well as the supporting cells in the brain are born," said Peter Nathanielsz, M.D., Ph.D., director of the Center for Pregnancy and Newborn Research in the Health Science Center School of Medicine.

Nathanielsz noted:

- In teenage pregnancy, the developing fetus is deprived of nutrients by the needs of the growing mother;
- In pregnancies late in reproductive life, a woman's arteries are stiffer and the blood supply to the uterus decreases, inevitably affecting nutrient delivery to the fetus;
- Diseases such as preeclampsia or high blood pressure in pregnancy can lead to decreased function of the placenta with decreased delivery of nutrients to the fetus.

Developmental programming of lifetime health has been shown to play a role in later development of obesity, diabetes and heart disease.

Indeed, in a second study, Texas Biomed scientists reported that inadequate nutrition during pregnancy predisposes offspring to becoming prediabetic before adolescence. Diabetes is an epidemic worldwide and a major health concern in San Antonio.

"This is the first time that diabetes has been shown to have prenatal origins in a primate model," said Texas Biomed's Anthony Comuzzie, Ph.D.

Published in the *American Journal of Physiology* and funded by the National Institutes of Health, the study was led by scientists from UTHSCSA.

Worldwide, diabetes is an escalating public health crisis. According to estimates from the World Health Organization, 366 million people will be diabetic by 2030, up from 171 million in 2000.

The study presents the strongest evidence yet that vulnerability to type 2 diabetes can begin in the womb, giving new insight into the mechanisms of a potentially devastating disease at the center of a worldwide epidemic. The study, conducted in 18 baboons, found that when mothers are even moderately undernourished while pregnant and



"THIS IS *the first time* THAT DIABETES HAS BEEN SHOWN TO HAVE PRENATAL ORIGINS IN A PRIMATE MODEL."

— ANTHONY COMUZZIE, PH.D.

breastfeeding, their offspring are consistently found to be prediabetic before adolescence.

POOR NUTRITION AND DIABETES

"Poor nutrition at critical periods of development can hinder growth of essential organs such as the pancreas, which sees a significant decrease in its ability to secrete insulin. Our study is the first to show in a primate that poor nutrition during fetal and early life can damage the pancreas and predispose to type 2 diabetes," said Nathanielsz, the senior author of the study.

Type 2 diabetes occurs when the body develops resistance to insulin, a hormone that regulates blood sugar. Although the body may initially compensate by secreting more insulin, eventually the pancreas cannot produce enough of it to keep blood sugar from rising. In poorly controlled diabetes, elevated blood sugar severely damages the heart, blood vessels, eyes, kidneys and nerves. The consequences can be fatal and include heart disease, stroke, amputations, blindness and kidney failure.

ADEQUATE VERSUS RESTRICTED DIETS

In the study, just before they reached puberty, six young baboons from nutritionally restricted mothers showed increases in fasting glucose, fasting insulin and other hallmarks of prediabetes. In contrast, the 12 young baboons whose mothers received adequate nutrition displayed none of these traits.

The central importance of this observation is that the mothers' food intake was only moderately restricted – similar to the decrease faced in the United States by many people living with food insecurity, Comuzzie said.

2011 DISCOVERIES:

A Reappraisal of Early Migration of the First North Americans

A DISEASE OR NORMAL BIOLOGICAL PROCESSES TO HELP DEVISE BETTER TREATMENTS. OCCASIONALLY THEY BECOME CONTEMPORARY EXPLORERS, REWRITING HISTORY EVEN IF THIS WAS NOT THEIR ORIGINAL INTENT. SUCH WAS THE CASE IN A PAPER AUTHORED BY TEXAS BIOMED SCIENTISTS IN THE FALL OF 2011 THAT DESCRIBED HOW AND WHEN THE FIRST HUMAN SETTLERS FIRST SET FOOT IN NORTH AMERICA.

"BY STUDYING THE VARIATIONS ACCUMULATED IN MITOCHONDRIAL GENOMES OVER TIME, WE CAN BUILD UP LINEAGES AND trace back the population history through the maternal lineage."

— SATISH KUMAR, PH.D.

Clues were extracted from the blood of San Antonio residents enrolled in the San Antonio Family Heart Study (SAFHS) by Texas Biomed's Satish Kumar, Ph.D.; John Blangero, Ph.D.; and their colleagues. The study, funded by the National Institutes of Health and the San Antonio Area Foundation, appeared in the journal *BMC Evolutionary Biology*.

Scientists can "read" the history of a people and even map their ancestors' journeys by studying

their genes. Human cells contain tiny structures called mitochondria. Like miniature engines, mitochondria convert food into energy that the body cells use for various functions. Because they are at the center of energy metabolism, mitochondria are very important to health. Mitochondria carry their own DNA and reproduce independently of the cell. The variations that occur in the mitochondrial genome affect energy production and other cellular functions.

"By studying the variations accumulated in mitochondrial genomes over time, we can build up lineages and trace back the population history through the maternal lineage," Kumar said.

GENES INHERITED MATERNALLY

The mitochondrial genome is inherited only from the mother. By studying it, scientists can trace the mother's family line far back in time and determine who the mother's female ancestors were and which traits they gave their descendants, as well as when and where they lived.

Kumar, the first author on the recent paper, has been studying the mitochondria of SAFHS volunteers to learn how their genes play a role in heart disease, diabetes, and obesity. He is also trying to understand their ancestors' history and the changes that happened in these genes over thousands of years. An expert in mitochondrial genes, Kumar had done similar work in years past, helping to trace the roots of Australian aboriginal tribes from India through southern Asia.

Why were the SAFHS participants good subjects for the new study? Many Mexican Americans are part American Indian. These ancestors came from Northeast Asia to North America across an ancient land bridge called Beringia, which used to connect Siberia and Alaska and is now covered by the waters of the Bering Sea. Most experts agree—based on genetic evidence, bones, artifacts, and the study of languages—that the ancestors of American Indians crossed the Bering land bridge, probably in pursuit of wild game.

NEW FINDING

But here's the new twist: Scientists had believed that, after leaving Asia, these ancestors were trapped in Beringia for 15,000 years by giant ice sheets and that their mitochondrial genes changed during this time. Kumar's work suggests that these ancestors did not stay in Beringia nearly that long. In fact, he says, SAFHS volunteers' mitochondrial genes suggest that their ancestors left Asia only about 20,000 to



RUSSIA

N O R T H A M E R I C A

Canad

Alaska

REWRITING HISTORY

- Scientists had believed that, after leaving Asia, the first human settlers to set foot in North America were trapped in Beringia for 15,000 years by giant ice sheets.
- In fact, Texas Biomed research suggests that these ancestors did not stay in Beringia nearly that long — less than 5,000 years.
- That is 10,000 years later than scientists had earlier believed. This new research suggests that they arrived in America from 16,000 to 20,000 years ago.

23,000 years ago. That is 10,000 years later than scientists had earlier believed. Kumar's research suggests that they arrived in America from 16,000 to 20,000 years ago.

"Beringia was more like a bus stop than a homeland," said John Blangero, Ph.D., director of Texas Biomed's AT&T Genomics Computing Center. "If they stopped, it was very brief—less than 5,000 years," agreed Kumar. "Otherwise, it is kind of a continuous movement to America. They were diverging from Siberian-Asian ancestors, coming to America."

Kumar and Blangero study the mitochondrial genes of hundreds of Mexican-American SAFHS volunteers to learn more about the genetic origins of diabetes and obesity. Many scientists have speculated that the high rate of diabetes in Mexican Americans is linked to their blood ties to American Indians, who have even higher diabetes rates.

FOUR TIMELINES

Kumar identified American Indian portions of the DNA from 215 local volunteers and combined that information with records of DNA collected by other researchers from American Indians and Asians. From those he could create four timelines, following each group through the years as new families branched off from old ones and spread into North, Central, and South America.

Exactly when each of the four groups crossed into the Americas isn't clear—probably between 16,000 and 20,000 years ago at the end of a period called the Last Glacial Maximum. In this study, Kumar ran three different estimates of human mitochondrial DNA mutation rates put forward by scientists each coming up with a range of dates showing a stop in Beringia of less than 5,000 years.

Having carved out new information about North America's original populations, now it's back to the lab for Kumar and Blangero to continue tracing the genetic variations that influence heart disease, diabetes, and obesity.

2011 DISCOVERIES:

Genes Found to Affect Levels of Antibodies



"OUR STUDY CLEARLY DEMONSTRATES THAT ANTIBODY LEVELS TO COMMON INFECTIOUS PATHOGENS ARE SIGNIFICANTLY HERITABLE and account for up to 40 percent of the individual variation IN ANTIBODY LEVELS IN THE PEOPLE STUDIED."

— HARALD GÖRING, PH.D.

LU. MONONUCLEOSIS. HERPES. PNEUMONIA. CHICKENPOX.

ALL OF THESE INFECTIONS CARRY SOME DEGREE OF INFLAMMATION, ACHES AND PAINS, AND OTHER UNPLEASANT SYMPTOMS AND CAN SOMETIMES LEAD TO SEVERE COMPLICATIONS. FOR YEARS, SCIENTISTS HAVE KNOWN THAT THE BODY PRODUCES ANTIBODIES TO FIGHT INFECTION AND THAT LEVELS OF THESE PROTEINS CAN PROVIDE INFORMATION ON PAST OR PRESENT EXPOSURE TO AN INFECTIOUS AGENT.

> Now, Texas Biomed scientists have, for the first time, found that for many of these infectious agents, an individual's genetic profile can contribute substantially to antibody levels. These scientists are currently conducting research seeking to identify the responsible underlying genetic variants. But even before they have completed this next step, their finding may have clinical significance.

> The study by Rohina Rubicz, Ph.D., and Harald Göring, Ph.D., funded by a four-year grant from the National Heart, Lung and Blood Institute, appeared in the journal *Human Heredity*. Coauthors include Charles Leach, M.D., and Ellen Kraig, Ph.D., of the University of Texas Health Science Center at San Antonio (UTHSCSA); Robert Yolken, M.D., of Johns Hopkins University; Nikhil Dhurandhar, Ph.D., of the Pennington Biomedical Research Center in Baton Rouge; and colleagues from the Department of Genetics at Texas Biomed.

"Our basic motivation in conducting this study was to determine if exposure to common infectious diseases may contribute to common diseases of aging such as obesity, diabetes, cardiovascular disease and atherosclerosis, which involves inflammation of the arterial walls," said Göring.

TESTS OF MEXICAN AMERICANS

In their study of 1,227 Hispanic volunteers enrolled in the San Antonio Family Heart Study (SAFHS), the scientists mainly used standard commercial testing methods and found that a person's genes play a significant role in how the immune system responds to 13 common disease-causing agents.

"Antibodies presumably do something, but it's not always clear why levels are higher in some people than in others," Göring said. "Practically speaking, antibodies are often used in clinical tests to diagnose infections. But if genes determine antibody levels, this might interfere with the actual diagnosis itself."

A high level of an antibody might mean that you are less efficient in dealing with an infection or that you have been infected more recently

or multiple times, said Rubicz. "But it can also mean the opposite, namely that your immune system has been highly successful in fighting the infection. You have to be careful in your interpretation of what differences in antibody levels actually mean. In other words, knowing that antibody levels are influenced by genetic differences does not directly address questions of infection susceptibility or resistance."

Although several studies have looked at the role of genes in people's responses to vaccines, few have looked at how they influence the body's defenses against natural infections, particularly in minority groups. The SAFHS began in 1991 in collaboration with researchers at UTHSCSA. It is the only large, population-based genetic study of risk for heart disease in Mexican-American families. It

ANTIBODIES IN THE BODY

An antibody is a large Y-shaped protein in the body used by the immune system to identify and neutralize foreign objects such as bacteria and viruses.



When someone has an infection, the body typically creates antibodies targeted at the invading viruses or bacteria in order to fight them off. The efficiency with which the immune system handles a particular infection can vary greatly between individuals. Tests are also often conducted to diagnose infectious diseases by measuring antibody levels rather than the

presence of a pathogen.

3

INFECTION

The scientists at Texas Biomed discovered that a patient's genetic factors can also play a substantial part in the amount of antibody levels to common infectious pathogens, and can account for up to 40 percent of the individual variation of these levels. focuses on 1,400 members of more than 40 large Mexican-American families, and even after 20 years the study is still going strong.

Because the volunteers are members of large families in which genetic relationships and thus also expected genetic similarities between individuals are known, the researchers were able to estimate the relative contribution of genetic factors to infection status and antibody levels. Infections with all of the 13 diseasecausing agents tested were shown to be significantly influenced by genes, except for adenovirus 36, which causes respiratory infections and has been linked to obesity, and herpes simplex virus 2, which is sexually transmitted. The findings were confirmed with samples from 648 volunteers from another local genetic study.

GENES AND ANTIBODY LEVELS

The authors note that antibody measurements are often interpreted as being indicative of pathogen exposure alone without explicitly acknowledging that innate characteristics of the patient, such as genetic factors, may influence antibody levels substantially. "Our study clearly demonstrates that antibody levels to common infectious pathogens are significantly heritable and account for up to 40 percent of the individual variation in antibody levels in the people studied," said Göring.

Because tests used to diagnose infectious diseases measure antibody levels, rather than the presence or absence of a pathogen, the tests could misrepresent whether an infection is present or not, Rubicz said. "At this point, we know there is a genetic component; and the next step is to identify the genetic variations that influence how an individual responds to infection."

2011 DISCOVERIES:

Texas Biomed Bolsters Program to Defend against Bioterror Threats

DECADE AFTER SEPTEMBER 11 AND THE ANTHRAX MAIL ATTACKS — WHICH KILLED FIVE PEOPLE — NATIONAL SECURITY EXPERTS CONTINUE WORKING ON STRATEGIES TO DETECT AND THWART A FUTURE BIOTERROR EVENT. BUT SCIENTISTS AT TEXAS BIOMED ARE AMONG ONLY A HANDFUL OF RESEARCH GROUPS WORKING TO ACTUALLY **PREVENT AND TREAT** THE DISEASES THAT COULD POTENTIALLY BE CAUSED BY BIOLOGICAL WARFARE, WHICH HAS BEEN DESCRIBED BY FBI OFFICIALS AS THE AGENCY'S MOST PRESSING CONCERN.

behavior make it a much better model than other larger and more aggressive nonhuman primates. The researchers have used the marmoset as a testing model for Eastern Equine Encephalitis virus, Lassa fever virus, and Ebola and Marburg virus. Their study, published in the Nov. 25, 2011, issue of the journal Virology, reported that the marmoset was susceptible to experimental infection with a family of deadly viruses, including Ebola virus and Marburg virus, and that symptoms were very similar to those seen in humans.

With the addition of a new scientist in 2011—Ewing Halsell Scholar Robert Davey, Ph.D.—Texas Biomed's Department of Virology and Immunology now has one of the most comprehensive programs anywhere to investigate treatments and vaccines for potential bioterror threats, said Jean L. Patterson, Ph.D., the department's chair. Research now under way in the department includes vaccine development, new detection and drug screening methods, and continued efforts to understand how viruses evolve and become potential threats.

VACCINES FOR BIOLOGICAL WEAPONS

Patterson has worked on the development of countermeasures against many potential biological weapons—known as "select agents"—that can cause lethal outbreaks. Her team includes Associate Scientist Ricardo Carrion, Ph.D., scientific manager of the biosafety level 4 laboratory; Scientist Luis Giavedoni, Ph.D., an immunologist; Assistant Scientist Anthony Griffiths, Ph.D., a molecular virologist; and primate center Veterinarian Kathy Brasky, V.M.D. They have helped develop three candidate vaccines against Ebola virus, two candidate vaccines against Marburg virus, and two vaccines against Lassa fever. Ebola, Marburg, and Lassa fever are particularly deadly agents that cause hemorrhagic fever. Lassa alone causes more than 500,000 infections annually in West Africa resulting in 3,000 to 5,000 deaths per year. The Defense Department and National Institutes of Health (NIH) are committed to developing an effective Ebola and Marburg vaccine by 2015, and Patterson's group is working with them toward this goal.

Along with Carrion, Patterson has developed the marmoset as a model for many infectious agents. This animal is a small, nonhuman primate that is not readily available to researchers, yet its size and

In addition, Carrion has started testing new detection methods for bioterror agents such as Crimean Congo hemorrhagic fever, an often deadly tick-borne disease seen in Eastern Europe, Asia, and Africa.

NEW DIAGNOSTICS

Andrew Hayhurst, Ph.D., is tackling the problem of how to develop antibody-based detection systems for viruses, toxins, and other targets of interest in as short a time as possible to cope with an "Andromeda strain" scenario. He has developed the "antibody pipeline," using Marburg virus as a model target, with the goal of producing a stopgap test to detect an unknown threat within 48 hours using inexpensive laboratory reagents available the world over.

Hayhurst has also developed a highly sensitive means of detecting the seven types of botulinum

These neuronal cells

how a monkey virus

nervous system jumps

that targets the

into humans.

are used to understand

neurotoxins (BoNTs) simultaneously. The finding may lead to improved techniques for testing water and food supplies should BoNTs be used as a bioterrorism weapon.

BoNTs are made by specific strains of the bacterium *Clostridium botulinum*, which are widely distributed in soil and aquatic sediment. Most cases of botulism are the result of foods stored improperly, which can encourage growth of clostridia and production of toxin that is then ingested. BoNTs are extremely potent and target the nervous system, resulting in paralysis that can be so severe as to require life support on a mechanical ventilator for weeks to months. Countermeasures to prevent and treat botulism, such as vaccines and therapeutics, are extremely limited. Consequently, the ability to detect these toxins in the environment is critically important.

BoNTs are about 100 billion times more toxic than cyanide, and the BoNT-detecting substances are antibodies—proteins made by the body to fight diseases—found in Ilamas. The Ilama antibodies, called sdAb or "nanobodies," are molecularly flexible, unlike conventional antibodies. "As such, sdAb may allow biosensors to be regenerable and used over and over without loss of activity," said Hayhurst. "Also, for some types of botulism toxins, conventional antibodies are not generally available, and we are filling this biosecurity gap."

Because some llama antibodies have been shown to have inhibitory activity and can block

toxin function, they also may play a role as part of a future anti-botulism treatment. This work was funded by the Defense Department's Defense Threat Reduction Agency Medical Diagnostics Program.

DRUG SCREENING

Davey, who began work in August, is using the Institute's biosafety level 4 (BSL-4) maximum containment laboratory to develop and optimize the identification of drugs to treat viruses such as Marburg and Ebola, among others.

"We have developed semi-automated approaches to drug screening that are safe and efficient and that work at high-containment. These include a microscope system that can automatically take photos of infected cells as well as computer software that we have customized to automatically identify infected cells and determine drug efficacy," Davey said.

"We are looking to see if related families of viruses behave in the same way. If they do, we may be able to identify one compound that attacks several families of viruses," he added.

This approach can drastically reduce by 90 percent the time spent finding effective drugs, compared with more traditional methods. Davey has also developed systems that can be used at low containment to help narrow down targets to a few thousand chemicals that can be tested in a few weeks. Davey is engaged in an ongoing project with a major drug screening facility at NIH with the goal of identifying new drugs against Marburg and Lassa fever viruses. The compounds that appear promising from this screen will be tested in the BSL-4 lab at Texas Biomed. Davey's team is also working with other labs in the department to help analyze data and tests—a project that is already reaping benefits in time and cost savings.

EVOLVING VIRUSES

Another important goal of biodefense work is to understand how viruses jump between species. Griffiths is uncovering how this occurs in the case of herpes B virus (BV), the monkey version of herpes simplex virus (HSV), the cause of cold sores in humans. BV can jump from monkeys, where it is benign, to humans, where it is highly lethal.

Emerging diseases frequently arise when a virus jumps to a new species; thus, understanding how BV jumps from a monkey to humans may provide important clues that will help predict when this may occur in the future.

"Basically, we are studying the evolution of viruses," Griffiths said. "HIV and flu viruses change very rapidly over time. That's important to know because you would not want to develop a therapy or vaccine against a region of the virus that changes rapidly."

Griffiths and his research team have been focusing on a newly recognized class of molecules known as microRNAs, which are encoded by some viruses and appear important for causing disease. In 2011, Griffiths' laboratory published a study in the *Journal of Virology* that used next-generation deep sequencing technology to discover BV-encoded microRNAs. Using this information, they investigated how these microRNAs were expressed, including studies using monkey tissues. This was the first in-depth study of viral microRNA expression, and it resulted in some interesting and surprising discoveries, including the first observation that microRNAs are incorporated into the virus particle.

Griffiths' study is the first to combine detailed herpes virus microRNA identification and expression in a naturally infected host, macaque monkeys, and normally infected cells. The work is so dangerous to humans that many of the experiments must take place in Texas Biomed's BSL-4 laboratory. The deep sequencing was funded by the Texas Biomedical Forum. Parts of the analyses that have relevance to diagnostic tests were funded by a supplement to the Southwest National Primate Research Center base grant and an NIH grant.

Once infected, one is never cured of any herpes virus, and there is strong evidence to suggest that microRNAs represent a key mechanism that permits the virus to hide from the immune system. The next steps in this research are to understand how this happens and to investigate whether the microRNAs function differently in human versus monkey cells.

While most HSV infections are self-limiting and fairly minor, HSV can lead to serious conditions, including encephalitis and blindness. Furthermore, HSV causes deadly diseases in immunocompromised patients, such as cancer patients receiving chemotherapy and transplant recipients receiving immunosuppressants. By studying a closely related virus in its natural host, Griffiths anticipates that his team will gain valuable insights that could lead to new therapies for HSV.

Although a major goal of this research is to improve the safety of animal care staff who work with macaque monkeys, it also has major implications for studies of other viruses, including those that represent bioterror threats.

As these lines of research progress during the years to come, San Antonio, the nation, and the world will become much safer due to the efforts of these scientists who are at the cutting edge of attacking the world's must unpredictable and deadly disease-causing agents.



CHAIRED BY JEAN L. PATTERSON, PH.D., THE DEPARTMENT OF VIROLOGY AND IMMUNOLOGY NOW HAS *one of the most comprehensive programs anywhere* TO INVESTIGATE TREATMENTS AND VACCINES FOR POTENTIAL BIOTERROR THREATS.

TEXAS BIOMED PROFILE

Danny Jones Guided Texas Biomed Library into the Digital Age

HEN HE BEGAN WORKING AT TEXAS BIOMED'S NORTHRUP MEMORIAL LIBRARY IN 2003, LITTLE DID DANNY JONES REALIZE THAT HIS REPUTATION WOULD DEPEND LARGELY ON A THREE- BY FIVE-INCH BLUE INDEX CARD.

One of Jones's first assignments as librarian was to find an easy alternative to the detested card that Institute scientists were required to fill out by hand in order to get a copy of an article in a process that could take a week or more. Jones found an electronic alternative, and within eighteen months scientists could request an article from their desktops with only a few mouse clicks. It was one of many Jones initiatives that guided a major overhaul of the library and brought it into the digital age. That he had gained the respect and admiration of the scientists was confirmed in the cheers and chuckles he received at an event recognizing Jones's retirement at the end of 2011.

Conversion from a classic physical library to an online virtual one was a milestone for Texas Biomed, said John Blangero, Ph.D., who heads the AT&T Genomics Computing Center. "This greatly facilitated scientific work at the Institute by removing barriers such as the nine-to-five workday for journal accessibility," he said. "Danny also provided us with new



tools that revolutionized the assessment of investigator productivity and comparability using bibliometric analysis."

Jones learned about the plans to redo the library shortly after arriving at Texas Biomed in 2003. "About two weeks after I got here, Vice President Gregory Patterson unrolled a floor plan and told me that my assignment was to plan the renovation of the library space," he said.

Along with physical renovation, the job would include converting to online access the card catalog, the checkout system, and the book and journal ordering system. Because the library remodeling project created an acute lack of space, Texas Biomed rapidly converted journals as much as possible to digital form and finished a year ahead of its peer institutions in digital conversion. Changing the journals from paper to online made it possible for researchers to have access to scientific journals at any time and from anywhere, rather than having to wait for copies during business hours.

"Our scientists are at the cutting edge of their areas of research, and they have to keep up," Jones said. "Our main job here is to make sure we have the journal content they need available when they need it."

In 2010, Texas Biomed investigators viewed or downloaded 25,835 full-text articles from the library's subscribed journals, plus uncountable additional articles from journals that are not subscribed.

"Danny really brought the library into the 21st century," said geneticist Laura Almasy, Ph.D. "During his tenure, he not only oversaw a renovation of the physical structure of the library, but also worked to move many library resources online, modernizing the way the library operated."

"CONVERSION FROM A CLASSICAL PHYSICAL LIBRARY TO AN ONLINE VIRTUAL ONE was a milestone for Texas Biomed."

– JOHN BLANGERO, PH.D.

Almasy and other scientists greatly appreciated the attention Jones paid to understanding scientific projects and thinking about new ways that the library could facilitate research at Texas Biomed.

"He was famous for the speed at which he delivered requests, particularly ones that required some time to sort out," said Jean L. Patterson, Ph.D., chair of the Department of Virology and Immunology.

The remodeled library includes a "collaboratory," a nine-seat room where colleagues can gather for webinars and staff training, creating Texas Biomed's first dedicated space for these activities. The library also includes the Vaughn Meyer Electronic Classroom, providing access to online teleconferences

and training on using electronic resources.

How did Jones wind up at Texas Biomed? He studied biology and chemistry as an undergraduate at Clemson University in South Carolina where he gained an appreciation for basic scientific research. He later earned a master's degree in librarianship at Emory University in Atlanta and came to San Antonio in late 1979. He worked at what is now the Briscoe Library at the University of Texas Health Science Center at San Antonio, where his wife, Rajia Tobia, is executive director of libraries. He first visited Northrup Library around 1983 when the first librarian, Mickey Funnell, hosted a meeting of local librarians.

"This was a doubly exotic experience for me," Jones said, "an opportunity to see the animals and to see the outstanding library, which was already recognized in the region for its comprehensive journal collection."

Jones left the Briscoe Library in 1998 and worked for HARRASSOWITZ, a German company that distributes European research books and journals

to North American libraries. He kept in touch with Funnell and her successor, Ruth Brooks, who let him know when she planned to retire. He had also come to know then Scientific Director Robert Shade, Ph.D.; and when the opening occurred, Jones was an obvious choice.

"In 2003, the kid-glove service commitment of the library was still evident, but it was still pretty much a pen-and-paper operation, and the time was ripe to bring it into the electronic era," Jones said. "We weren't going to have a place to put print journals during the remodeling process, so we forged ahead and over two years converted about 95 percent of our subscriptions to online access, telling publishers we didn't want them to send the print journals."

"To my knowledge," he said, "no library in the country had committed to online-only subscriptions at the time, so it was a bit of a gamble for us. And by eliminating much of the print journal collection, we were able to make space for the classroom, the collaboratory, and a variety of individual and group seating areas."

More recently, Jones took on the restoration of the papers of Texas Biomed founder Tom Slick Jr. The papers were in a shed where they had been stored for years near animal feed and were exposed to humidity and rodents. Jones worked with preservation specialists who used a freezing chamber, radiation, and other methods to kill and remove mold spores and insect infestation. He then helped arrange for the papers to be donated to the University of Texas at San Antonio Library Archives and Special Collections. They will be preserved in perpetuity and made available for scholarly research.

In retirement, Jones and his wife plan to travel around the United States and to Europe and Asia. That may include Japan, where one of their two sons has applied for a job teaching English. At home, Jones enjoys gardening and has developed an interest in native plants, with plans to turn his back yard into a laboratory to see what he can grow.

Of his time at Texas Biomed, Jones said that the scientists "are doing things that nobody has done before, and it is very interesting to be around people like that." Especially those who are forever grateful that the blue index cards are no more.



1 year

how much Texas Biomed finished ahead of its peer institutions in digital conversion

25,835

number of full-text articles downloaded in 2010

YEAR IN REVIEW

ANY EVENTS DURING 2011 MARKED TEXAS BIOMED'S CONTINUING SUCCESS BOTH IN EXPANDING ITS SCIEN-TIFIC RESEARCH AND IN SPREADING ITS REPUTATION IN SAN ANTONIO, TEXAS, THE NATION, AND BEYOND. IMPORTANT TO THIS EFFORT WAS THE UNVEILING OF THE INSTITUTE'S NEW NAME.

Other highlights included growing recognition of accomplishments by Texas Biomed staff members, campus visits by representatives of the San Antonio congressional delegation, and the addition of a high-profile infectious disease researcher to the Department of Virology and Immunology.

NEW NAME

On February 1, the Southwest Foundation for Biomedical Research became the Texas Biomedical Research Institute. The new name recognized the pioneering, independent, and courageous legacy that is so much a part of Texas history. It also overcame continuing name confusion with sister organization Southwest Research Institute, eliminated the word "foundation," which misconstrued Texas Biomed's primary mission of discovery, and helped provide a more fitting nickname than "SFBR" or "Foundation." Established in 1941 as the first and largest of its kind in Texas, the Institute has earned and continues to merit the goodwill associated with this truly vibrant and visionary state. The new nickname, "Texas Biomed," and tagline, "Enhancing lives through discovery," clearly

underscore this message and inform the public and the broader scientific community.

"The new name comes at a fortuitous time, when elements of a programmatic and facilities master plan have been developed and approved that will transform the campus and bring added power to the research enterprise," said Texas Biomed Board Chair J.R. Hurd.

With the new name also came a new Web site with rotating banner stories about the work of the Institute, a new seven-minute video explaining past and present research projects, and new campus wayfinding signs and banners to reinforce the new brand.

NEW NAME, NEW MESSAGE

The new name recognizes the pioneering, independent, and courageous legacy that is so much a part of Texas history, while the tagline reflects the goal to inform the public and the broader scientific community.



OUTREACH TO SAN ANTONIO AND BEYOND

During 2011, Texas Biomed President and CEO Kenneth P. Trevett strengthened collaborations with other research organizations and enhanced the organization's visibility within the community. He serves on the board of the Texas Research & Technology Foundation and on the advisory boards of the Southwest Research Institute and South Texas Accelerated Research Therapeutics. He is also a member of the executive committee of United Way.

In January, Trevett was elected to succeed Henry Cisneros as chair of BioMed SA. This nonprofit organization seeks to accelerate the growth of San Antonio's biomedical sector, create regional economic benefit, and contribute to the health of San Antonio and beyond by establishing the city as a leader in health care and bioscience.

Trevett promised to "aggressively and productively advocate for San Antonio's biomedical sector. I am convinced that San Antonio can and will be the next hub for biomedicine in this country, and in

" I AM CONVINCED THAT SAN ANTONIO CAN AND WILL BE *the next hub for biomedicine* IN THIS COUNTRY..."

- KENNETH P. TREVETT

accordance with our newly adopted strategic plan, BioMed SA will lead the effort for San Antonio's recognition as a global leader in health care and bioscience," he said.

Cisneros, a former San Antonio mayor and Secretary of Housing and Urban Development, founded BioMed SA in 2005 and served as board chair from its inception.

Texas Biomed is an active member of the Association of Independent Research Institutes (AIRI) and played a significant role at its 2011 annual meeting. Gregory



Gregory M.L. Patterson, Ph.D. (left), vice president of research operations, and Sarah Williams-Blangero, Ph.D. (right), chair of the Department of Genetics

M.L. Patterson, Ph.D., Texas Biomed's vice president of research operations, was elected AIRI president-elect. He had served as secretary of its board of directors and member of the annual meeting program committee.

In addition to being a member of Research!America, a nonpartisan alliance in support of public education and advocacy to make health research a higher national priority, Texas Biomed is also a member of the Scientists' Center for Animal Welfare (SCAW). Anthony Comuzzie, Ph.D., a Texas Biomed geneticist, served as a member of the SCAW board of trustees.

Texas Biomed opened its doors during the first three months of 2011 to seven classes of high school seniors when the Institute's Forum hosted its annual tours for advanced biology and chemistry students. The students learned about exciting careers in science by viewing a video overview of the Institute, visiting the AT&T Genomics Computing Center and the Southwest National Primate Research Center, and speaking with Texas Biomed scientists working on hepatitis C, heart disease,

diabetes, obesity, and other health problems.

> In addition, Sarah Williams-Blangero, Ph.D., chair of the

Department of Genetics, was designated a Health Care Hero by the *San Antonio Business Journal*. The annual award honors leaders in the city's health care and biomedical fields. Williams-Blangero was recognized for her work in the field of infectious disease genetics.

The Institute hosted visits by officials of the Canadian government, representatives of several members of the San Antonio congressional delegation, and a number of prominent scientists.

In April, Mona Ayoub, vice consul and trade commissioner for life science at the Canadian consulate in Houston, visited

Year in Review (continued,

and toured the campus. Her goal was to gain a better understanding of Texas Biomed's research program and discuss possible international collaborations.

Other visits throughout the year included staff members from the offices of Rep. Lamar Smith, Rep. Francisco Canseco, Sen. Kay Bailey Hutchison, and Sen. John Cornyn. Institute president Kenneth P. Trevett presented an overview of Texas Biomed, and the visitors toured the biosafety level 4 laboratory, AT&T Genomics Computing Center, and animal areas.

Lee Hood, M.D., Ph.D., the father of molecular medicine and founder and director of the Institute for Systems Biology in Seattle, visited Texas Biomed and met with department chairs and other scientists to discuss their work and possible collaborations.

EWING HALSELL SCHOLAR

In August, Robert Davey, Ph.D., formerly an associate professor at the University of Texas Medical Branch in Galveston, joined Texas Biomed in the position of scientist in the Department of Virology and Immunology. San



Antonio's Ewing Halsell Foundation donated \$2 million to fund the new position, which also carries the name "Ewing Halsell Scholar." Davey's work focuses on the identification of factors important for establishing infection by retroviruses and filoviruses, which cause hemorrhagic fever. He is also performing drug screens in collaboration with the National Institutes of Health (NIH), using 350,000 small molecules to help identify new drugs for prevention and treatment of disease caused by some of the world's most dangerous viruses.

TOM SLICK PAPERS TO UTSA

Also in August, Texas Biomed helped arrange for the family of Thomas Baker Slick Jr., founder of the Texas Biomedical Research Institute and other science organizations in San Antonio, to donate his papers to the University of Texas at San Antonio Libraries Special Collections.

The 75 boxes contain papers related to Texas Biomed, the Southwest Research Institute, the Mind Science Foundation, and other partnerships and corporations. The papers include documents relating to the disbursement of the estate assets and the trusts of Slick, who died in a plane crash in 1962 at age 46. The papers will be available to scholars and researchers who are interested in the origins of the biomedical and scientific enterprise in San Antonio and South Texas, the oil and gas industry, the history of the research institutions that Slick established, and his varied other interests.

Slick left a vast set of correspondence from 1938 to 1962, and this donation represents the first time, after nearly 40 years, that it will be available.

REMEMBERING FRIENDS

Three long-time members of the Texas Biomed Board of Trustees passed away during 2011. Charles Foster, who had a 41-year career in the telecommunications industry, served on the board's executive committee as well as several search committees, playing a key role in many big decisions. Louis Stumberg, a food industry pioneer, played an important role in defining board discussions and helping to clarify complex issues. Hugh Half Jr., a philanthropist and outdoorsman, clearly understood the important role of the institute on a national and international level.

Much-loved long-time employee Leroy Wertz passed away shortly after retiring at the end of 2010. He held a variety of positions during a 43-year career at Texas Biomed, including nearly two decades in the Shipping and Receiving Department, where he became known as *the man* who delivered the mail.

CHIMPANZEES IN RESEARCH

Late in the year, the National Academy of Sciences' Institute of Medicine issued a report requested by the NIH that put new limits on the future use of chimpanzees in biomedical research. The issue was raised earlier in the year when NIH put on hold the scheduled transfer of about 200 chimpanzees from Alamogordo, New Mexico, to Texas Biomed's Southwest National Primate Research Center. Issues related to the transfer prompted many stories in the national media, including the *New York Times, Washington Post*, McClatchy News Service, and NBC's Rock Center with Brian Williams. NBC spent six days filming at Texas Biomed for a program that aired in January, 2012.

MOVING ON

In 2011, four long-time Texas Biomed staffers retired, including geneticist David Rainwater, Ph.D., and Facilities Director Lee Bricker. In addition, Administrative Assistant Cindy Calderon, who coordinated the activities of the Institutional Animal Care and Use Committee,

Chimpanzees: Late in the year, the National Academy of Sciences' Institute of Medicine issued a report that put new limits on the future use of chimpanzees in biomedical research.

retired after 23 years. Librarian Danny Jones (see profile, page 26) retired after nine active years of bringing the library into the digital age.

LOOKING AHEAD

Texas Biomed's leadership has enabled the organization to thrive during an era of limited funding from the NIH. The future for government biomedical research spending remains uncertain. The Institute is now embarking on a plan to attract top-notch scientists, improve its physical plant and create optimal conditions in which to conduct first-rate science and diversify and expand its portfolio of research partners. As Texas Biomed moves forward into 2012 and beyond, it will continue to identify ways to build on its record of research accomplishments and to enhance its ability to advance the health of people everywhere.

FINANCIALS

Financial Performance in 2011

IN RESPONSE TO A CHALLENGING YEAR IN 2010, THE BUDGET FOR 2011 WAS PROJECTED TO BE NEUTRAL IN CASH GENERATED FROM OPERATIONS. SENIOR MANAGEMENT IMPLEMENTED NEW FINANCIAL MONITORING PROCESSES AND ADOPTED COST CUTTING MECHANISMS TO STRENGTHEN FINANCIAL RESULTS.

Such programs included a voluntary early exit program that will save approximately \$500,000 in each future year as well as one-time reductions in planned purchases. As a result, Texas Biomed was able to achieve gains from operations of nearly \$200,000, an improvement over what was budgeted.

Ernst & Young's audit of Texas Biomed's operations for the fiscal year ending December 31, 2011, is expected to be completed in late spring 2012. As in prior years, no material adjustments are expected. Because of the audit schedule, the figures displayed here have not been independently audited. The final audit for 2011 will available in the summer of 2012. Copies may be obtained through the Institute's Vice President for Finance and Administration and Chief Financial Officer, Jeannie Frazier (210-258-9404).

Three-quarters of Texas Biomed's funding in 2011 came through highly competitive, peer reviewed research grants and contracts from the National Institutes of Health and other federal agencies. Augmenting this, approximately 3 percent of the Institute's operating revenue came from commercial contracts with biotechnology firms and pharmaceutical companies.

3.1%

Philanthropy continues to play a much needed role in the research that Tom Slick envisioned when he founded the organization in 1941. As the revenue chart indicates, philanthropic sources provided about 20 percent of the Institute's annual budget, funding important research and facilitating the purchase of state-of-the-art equipment.

This year, using funds generously contributed by the Ewing Halsell Foundation, Robert Davey, Ph.D., a noted virologist, was recruited. Financial support such as this from donors enables Texas Biomed to attract and retain the world's top scientists, equipping state-of-the-art laboratories, and providing the opportunity to work on innovative pilot projects to explore new ways to understand and eliminate diseases. Private gifts also leverage significant additional investment by allowing investigators to compete successfully for prestigious



Financial Performance (continued)

foundation grants that do not cover the full cost of research. Important Texas Biomed sources of philanthropic funding include the Golden Circle, the Founder's Council, the Forum, and annual contributions from Argyle members.

Research at Texas Biomed is also made possible through the earnings on previous philanthropic gifts to the Institute's endowment, accounting for 6

percent of revenue. During the course of 2011, Texas Biomed's endowment hit its all-time high, over \$96 million, before settling back to its current value of just under \$91 million. The Investment Committee of the Board of Trustees continues its efforts to both increase the endowment balance and provide protection from market swings.

As in prior years, Texas Biomed received significant royalties on oil and gas properties that had previously been contributed by donors. This revenue, comprising 4 percent of total revenue, provides a stable source of funding at a time when the competition for federal grant funding is increasing.

Texas Biomed's leadership is working to reduce expenses and increase revenue in 2012. Successful negotiations on health care premiums will lower costs to Texas Biomed by nearly \$500,000 in 2012, as well as provide new choices and reduced premiums





for employees. With efforts such as these, along with the support of a strong donor base, Texas Biomed will continue its positive financial position into the future.

FEDERAL RESEARCH GRANTS AND CONTRACTS	PRINCIPAL INVESTIGATOR	LENGTH	TOTAL AMOUNT TO TEXAS BIOMED
National Institutes of Health (NIH) NIH-Owned Chimpanzee Research Resource at the SNPRC	Dr. John L. VandeBerg	5 yrs	\$19,117,453
NIH Mapping Drug Resistance Genes in Plasmodium falciparum	Dr. Timothy J. C. Anderson	5 yrs	\$3,467,918
NIH Bone Structure Integrity Profiling to Advance Skeletal Genetics and Biomechanics	Dr. Lorena M. Havill	5 yrs	\$3,082,796
NIH/Emory University A Dual Vaccine Strategy Against Filovirus Infection	Dr. Jean L. Patterson	5 yrs	\$2,676,147
Defense Threat Reduction Agency Identification of Broad Spectrum Targets for Therapeutic Intervention Against Crimean Congo, Ebola, and Lassa Hemorrhagic Fever Virus Infection by High Throughput siRNA Screening	Dr. Robert Davey	5 yrs	\$2,478,968
NIH The Innate Immune Response in the Marmoset Model of GBV-B Infections: A Surrogate Model for HCV and a Primate Model for Gene Knockdown	Dr. Robert E. Lanford	5 yrs	\$2,290,675
NIH Genetic Analysis of Host Specificity in Schistosoma mansoni	Dr. Timothy J. C. Anderson	3 Yrs	\$1,786,970
NIH Gene Networks for Differential Risk of Kidney Damage by Long-Term Diabetes	Dr. Jack Kent Jr.	4 yrs	\$1,589,350
NIH 2/2 – An Integrative Genetic Investigation of Schizophrenia	Dr. Harald H. H. Göring	5 yrs	\$1,074,600
NIH Development of a Vaccine to Protect Monkeys from Herpes B Virus Infection	Dr. Anthony Griffiths	2 yrs	\$482,625
NIH/Harvard University Self-Injurious Behavior and Primate Well-Being	Dr. Corrine K. Lutz	5 yrs	\$235,546
NIH/University of Oklahoma Health Science Center Telomere Attrition and Diabetes Risk in American Indians	Dr. Shelley Cole	3 yrs	\$229,821
NIH Luminex Technology for the Quantification of Cytokines in Nonhuman Primates, Supplement	Dr. Luis D. Giavedoni	4 mos	\$203,561
NIH Diet and Genotype in Primate Atherosclerosis (Diversity Supplement, Cost Extension) Supplement	Dr. G. Karere Dr. John L. VandeBerg	2 yrs	\$167,760
NIH/Nationwide Children's Hospital HCV-Specific T Cell Response	Dr. Robert E. Lanford	6 mos	\$150,000
NIH/Sepulveda Research Corporation Mechanisms of Race-Based Differences in Factor VIII Immunogenicity in Hemophilia (ARRA RC2)	Dr. Shelley Cole	1 yr	\$94,874
NIH/University of Puerto Rico Establishment and Maintenance of a Closed CPRC SPF Colony	Dr. Sarah Williams-Blangero	4 yrs	\$81,938

FEDERAL RESEARCH GRANTS AND CONTRACTS	PRINCIPAL	I ENGTH	TOTAL AMOUNT TO
NIH/University of Texas Health Science Center, San Antonio Effects of Rapamycin on a Small, Short-Lived, Primate, the Common Marmoset	Dr. Kathleen M. Brasky	1 yr	\$63,518
NIH/University of Texas Medical Branch, Galveston Development of Antibody-Based Diagnostic Assay for Filoviruses	Dr. Robert Davey	1 yr	\$33,561
Department of Defense/Operational Technologies Corporation Handheld Aptamer-Magnetic Bead-Quantum Dot Sensor for Rickettsiae	Dr. Ricardo Carrion Jr.	6 mos	\$29,646
NIH/Medical College of Wisconsin National Children's Study – Vanguard Center	Dr. Melanie Carless	8 mos	\$24,068
NIH/Planet Biotechnology Rabbit B. anthracis Challenge Study	Dr. Ricardo Carrion Jr.	4 mos	\$20,002
NIH/Medical College of Wisconsin National Children's Study – Vanguard Center	Dr. Melanie Carless	7 mos	\$19,765
NIH/Texas Tech University Population-Based Mapping of Schizophrenia Genes	Dr. John Blangero	7 mos	\$17,767
NIH Marburg Virus Drug Testing	Dr. Jean L. Patterson	3 mos	\$15,037
NIH Ebola Virus Testing	Dr. Jean L. Patterson	3 mos	\$11,579
U.S. Army Feasibility of Lower Body Negative Pressure as a Hypovolemia Model in Baboons, Supplement	Dr. Robert E. Shade	1 yr	\$10,783
World Health Organization Development of Biomarkers for Praziquantel Resistance in Schistosomiasis	Dr. Timothy J. C. Anderson	2 yrs	\$10,000
NIH/University of Washington Semen Collection - Baboons	Dr. Kathleen M. Brasky	11 mos	\$3,024
National Science Foundation/Trinity University Development of Hemispheric Specialization in Capuchin Monkeys, Supplement	Dr. Karen Rice	1 yr	\$2,436
NIH/University of Washington Using Genomics and Proteomics to Identify Primate Seminal Fluid Proteins	Dr. Kathleen M. Brasky	1 yr	\$2,330
NIH/University of Texas Medical Branch, Galveston Development of Bupropion for Smoking Cessation During Pregnancy, Supplement	Dr. Karen Rice	3 yrs	\$1,785

TOTAL FEDERAL Research grants and contracts

^{\$}39,476,303

ACADEMIC RESEARCH GRANTS AND CONTRACTS	PRINCIPAL INVESTIGATOR	LENGTH	TOTAL AMOUNT TO TEXAS BIOMED
University of Texas Health Science Center, San Antonio MRI Imaging in Marmosets Supplement	Dr. Kathleen M. Brasky	10 mos	\$74,615
University of Texas Health Science Center, San Antonio A Nonhuman Primate Model of Teenage Pregnancy	Dr. Robert E. Shade	11 mos	\$43,923
Duke University Animal Sale	Dr. Karen Rice	5 mos	\$38,327
University of Michigan Feasibility and Effects of Levonorgestrel-intrauterine System (US) Placement in Baboons	Dr. Robert E. Shade	1 yr	\$36,949
Boston University Male Baboon Purchase and Testing	Dr. Ricardo Carrion Jr.	7 mos	\$29,333
University of Texas Health Science Center, San Antonio Marmoset Biological Tissue Collection, Supplement	Dr. Kathleen M. Brasky	2 mos	\$29,302
Baylor Research Institute <i>Reversal of STZ-Induced Diabetes Using Ultrasound Destruction of Microbubbles for the Delivery of</i> <i>Genes to the Baboon Pancreas, Supplement</i>	Dr. Anthony Comuzzie	1 mo	\$26,819
University of Texas Health Science Center, San Antonio Brain Imaging of Chimpanzees	Dr. Kathleen M. Brasky	2 mos	\$22,037
International AIDS Vaccine Initiative To Demonstrate the Presence of Memory B–Cells in Baboons Previously Immunized with a HIV Vaccine	Dr. Krishna K. Murthy	1 yr	\$15,499
University of Texas Health Science Center, San Antonio Marmoset Biological Tissue Collection	Dr. Kathleen M. Brasky	1 yr	\$1,028
University of Missouri Hip Joint Mobility and Locomotor Diversity in Anthropoids	Dr. Karen Rice	1 yr	\$405

TOTAL MISCELLANEOUS Research grants and contracts

\$318,237

			TOTAL AMOUNT TO
Robert J. Kleberg Jr. & Helen C. Kleberg Foundation		1 yr	¢ 494 427
Cowles Memorial Trust Postdoctoral Fellowship (Cheeseman)	Dr. Gregory M. L. Patterson	1 yr	\$56.779
Society for Women's Health Research Genetic Architecture of Knee OA: Lessons from Healthy Joints in Animals of Advanced Age	Dr. Lorena M. Havill	1 yr	\$48,851
Jean Marmion Genetic Determinants of Multiple Sclerosis, Supplement	Dr. John Blangero	1 yr	\$40,000
Texas Biomedical Forum Application of Exome Sequencing to Identify Genetic Variants Contributing to Schizophrenia and Related Phenotypes	Dr. Mark Kos	1 yr	\$35,000
Texas Biomedical Forum Gossypin, a Novel Dual Inhibitor of BRAF V600e and CDK4 Kinases in Melanoma Management	Dr. Hareesh B. Nair	1 yr	\$35,000
Texas Biomedical Forum Single Cell Genomics for Malaria Parasites	Dr. Ian H. Cheeseman	1 yr	\$35,000
William and Ella Owens Foundation In Vitro Therapeutic Regulation of a Gene that Modulates HDL Cholesterol	Dr. Laura A. Cox	1 yr	\$34,863
Texas Biomedical Forum <i>Pharmacogenetics of Glucuronidation in American Indians</i>	Dr. Phillip E. Melton	1 yr	\$34,141
Texas Biomedical Forum Functional Neuroimaging in Response to Food Challenge	Dr. Joanne E. Curran	1 yr	\$33,000
William and Ella Owens Foundation Fine Mapping of Contact Sites within the Ebola Virus Nucleoprotein	Dr. Daniel A. J. Mitchell	1 yr	\$26,620
Joe and Jessie Crump Foundation Advancing the Models for Liver Cancer	Dr. Robert E. Lanford	1 yr	\$25,000
Texas Biomedical Forum Prevalence and Plasticity of Stem Cells in Knee Osteoarthritis	Dr. Heather Coan	1 yr	\$18,341
Cowden Charitable Foundation Assessing Transcriptional Profiles of the Decidua in Pre-eclamptic and Nonpre-eclamptic Pregnancies	Dr. Matthew Johnson	1 yr	\$10,000
American Association of Physical Anthropologists Reconstruction of Migration Patterns in Mennonite Communities Using Molecular Markers: Y-Chromosome Perspective	Dr. Phillip E. Melton	1 yr	\$5,000

TOTAL FEDERAL RESEARCH Grants and contracts	^{\$} 39,476,303
TOTAL ACADEMIC RESEARCH Grants and contracts	\$318,237
TOTAL PHILANTHROPIC Research grants	\$922,032
TOTAL COMMERCIAL Research Grants and contracts	^{\$} 1,215,176
TOTAL GRANTS AND CONTRACTS	
AWARDED TO TEXAS BIOMED IN 2011	\$41,931,748

TOTAL PHILANTHROPIC Research grants



WHY SUPPORT TEXAS BIOMED?

It's a fact of life THAT GRANT AND CONTRACT INCOME ARE INSUFFICIENT FOR TEXAS BIOMEDICAL RESEARCH INSTITUTE TO ACHIEVE ITS IMPORTANT MISSION.

Since the organization's founding in 1941, giving has been a powerful enabler of progress, making philanthropy one of the cornerstones of this institution's success. Here are a few examples of how financial support can make all the difference to Texas Biomed scientists:

\$1=\$12 LEVERAGE. On average, for every \$1 contributed, Texas Biomed scientists gain another \$12 in competitive grant support, making Institute researchers among the most productive anywhere.

CRITICAL PROGRAMS AND PROJECTS.

The proceeds from research grants and contracts represent the primary funding source of Texas Biomed, totaling about 75 percent of revenue. The remaining funding comes from endowment income and current donations.



KEY RESEARCH VENTURES. Donations fund pilot studies and the recruitment of key scientists, each of which encourage bold initiatives by Texas Biomed scientists.



EXTRAORDINARY RESOURCES. Texas

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

TECHNOLOGY. The latest advances in technology make modern research more productive. The high cost of the newest technology usually requires philanthropic support.

Unlike some research organizations, Texas Biomed does not have patient or tuition revenue to fund capital and operating expenses. Donations are critical for funding new programs and capital purchases.

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

Make the difference.



TEXAS BIOMEDICAL FORUM

SUZANNE DABBOUS, PRESIDENT, TEXAS BIOMEDICAL FORUM HE NEWLY NAMED TEXAS BIOMEDICAL FORUM HAD ANOTHER EXCITING YEAR IN 2011. THE NAME CHANGE WAS OFFICIALLY ADOPTED IN THE SPRING BY A UNANIMOUS VOTE OF THE TRUSTEES. AND ALTHOUGH THE NAME HAS CHANGED, OUR MISSION TO SUPPORT TEXAS BIOMED AND THE NUMEROUS MEMBER VOL-UNTEERS WHO MAKE THIS SUPPORT POSSIBLE REMAINS STEADFAST.

The annual spring lecture luncheon, featuring Madeleine Reichert, D.M.H., a nationally respected and locally loved family psychologist, sold many seats at The Argyle's Slick-Urschel room. Her lecture, "Can I Be Lady Bountiful but Still Draw a Boundary?," was met with applause, laughter, and a few tears.

Also during the luncheon, winners of the Science Education Awards were announced. The Science Education Award recipients are local teachers who submit proposals for up to \$7,000 to supplement a specific science project. Given jointly by the Forum and the V.H. McNutt Memorial Foundation, this program is a favorite of many Forum members. The L.D. Ormsby Foundation also supports the science education awards by funding stipends to applicants. In total, \$20,000 in awards was granted this spring.

Thankfully, some things do not change. The year's annual spring gala at The Argyle on May 1 was no exception. The Argyle, transformed into A Shanghai Affair with "AS A DIRECT RESULT OF THESE FORUM GRANTS OVER THE YEARS, TEXAS BIOMED HAS BEEN AWARDED *more than \$23 million* IN LARGER, FEDERAL GRANTS SINCE 1999."

brilliant red carpet and oriental decor, was completely sold out. More than \$185,000 raised for the Texas Biomedical Research Institute was awarded to scientists in seed grants. As a direct result of these Forum grants over the years, Texas Biomed has been awarded more than \$23 million in larger, federal grants since 1999. This year's grant recipients and their research can be found on page 36. In May, Karen Lee Zachry, the Forum's 41st president, handed over not one but two gavels. The old gavel with the old name and the new gavel with the new name were physical reminders to all those present

that this was a time of change. The Forum could not have asked for a better president in 2011, particularly in light of the name change. Karen Lee Zachry, a lawyer, educator, and professional, was the perfect fit to make the many changes seamless. Following the meeting, many board members attended an intimate luncheon.

The Forum returned in the fall to several challenges relating primarily to the name change. Although the name change was official for the Forum, the papers filed with the IRS for 501(c)(3) charity status were still pending official approval. Thanks to the perseverance of board members and the generosity of the Institute, the issues, mostly related to mailings, were resolved.

A fall kickoff party for the spring gala was held at The Argyle on September 28 and unveiled the 2012 theme: Dewali, popularly known in India as the festival of lights, a celebration of the triumph of good over evil. The gala will be held May 5, 2012, at The Argyle. In October, Texas Biomed Vice President for Institutional Advancement Corbett Christie and Terry Gouger, a previous Forum president, worked with our trustees to initiate a change in the format for the annual Insider's Tour. Previously held at the Institute, this year's Insider's Tour was held at The Argyle and paired scientists with Forum members for a personal account of ongoing research.

On November 16, Bangles Boots and Bags, the annual Girls Night Out event graciously hosted by Julian Gold, was stepped up a notch to include a trunk show by jewelry designer Elizabeth Showers and a raffle with prizes including a \$1,200 Emilio Pucci shopping spree. The event generated a total of \$3,000.

The fall lecture luncheon on November 9 with Texas Biomed Chief Scientific Officer John L. VandeBerg, Ph.D., gave members of the Forum a fascinating look into the future of medicine and research.

December is our slowest time at the Forum. Last year, we started a new tradition by having a gathering during the holiday season, and in 2011 trustees and their spouses attended a similar event.

In its 41st year, the Forum has undergone many changes besides its renaming.

We are in the midst of an ongoing transition to online services. Members can now purchase gala raffle tickets, give gala grants, receive a newsletter, reserve a luncheon seat, and renew their memberships online. This promises not only to improve the efficiency of the Forum, but insures our future success in upholding our purpose: to support the Texas Biomedical Research Institute through community relations, volunteer service, and fund raising.





FOUNDER'S COUNCIL

- Lorena M. Havill, Ph.D., for a camera kit for visualizing cells and how they respond to various treatments.
- Melanie Carless, Ph.D., for a specialized oven for the study of samples in cardiovascular disease research.
- Joanne Curran, Ph.D., for an incubator system for use in studies related to heart disease, diabetes, and arthritis.
- Laura Cox, Ph.D., for a device used to understand the genetic mechanism that regulates variation in heart disease and hypertension.
- Luis Giavedoni, Ph.D., and Vida Hodara, Ph.D., for an instrument to identify and purify gene fragments.
- Anthony Griffiths, Ph.D., for a cell counter for studies of how viruses jump between species.



Today, the young men and women of the Founder's Council, whose ages of 25 to 46 reflect Slick's visionary initiative to found the Institute at age 25, provide financial support for scientific research at Texas Biomed.

To advance the awareness of Texas Biomed and its research efforts, the Founder's Council hosted three lecture luncheons in 2011 featuring Institute scientists as speakers. The signature event, "Dining and Discourse," allowed members to

2011 FOUNDER'S COUNCIL MEMBERS Mr. Clay Aderholt Ms. Jenni Allen

Mr. Joshua Allen

Mr. David Altgelt Dr. and Mrs. Garrett K. Andersen Mr. Jeffrey Anderson Mr. and Mrs. Brian Patrick Arriaga Sr.

Mr. and Mrs. James Avery Ms. Tracy Avery Mr. and Mrs. Michael A. Bacon Mr. Jeff P. Bailey Ms. Jamie Bauer

participate in lively discussions over dinner

with the Institute's leading researchers.

informal social mixers to network and

fostered through this energetic and

Members' annual donations of \$135

enthusiastic group of supporters.

Founder's Council members also enjoyed

meet colleagues. Texas Biomed is stronger

because of the visionary young leadership

per individual, \$195 per couple, and \$500

or \$1,000 at the higher levels of giving,

Mr. Matthew M. Bell Mr. and Mrs. Eduardo Berdeque Ms. Catherine Bishop Mr. Geoffrey A. Bley Mr. John Bozada

Mr. C. Dawson Bremer

THE FOUNDER'S COUNCIL ENCOURAGES TODAY'S YOUNG LEADERS TO LEAVE A LEGACY INSPIRED BY TEXAS BIOMED'S FOUNDER, TOM SLICK. IN ESTABLISHING THE INSTITUTE, SLICK ENVISIONED "A GREAT CENTER FOR SCIENTIFIC PROGRESS THROUGH **BIOMEDICAL RESEARCH.**"

> fund competitive grants to Institute researchers for the purchase of key pieces of scientific equipment.

At the holiday party, Founder's Council President Craig Browning presented an additional check in the amount of \$37,000 to Kenneth P. Trevett, president of Texas Biomed, for ongoing research at the Institute. These monies signify donations by members at the Explorer and Adventurer levels.

Mr. Jeffrev Brouillard Mr. J. Craig Browning Jr. Dr. and Mrs. John Browning Mr. Todd Burchett



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Grant Awards (continued

- Robert Lanford, Ph.D., for an instrument to test viral proteins and the immune response to viruses.
- Melissa de la Garza, D.V.M., for a stretcher to aid in the transportation of research animals.
- Qiang Shi, Ph.D., for a microscope viewing screen used in the study of genetic determinants of atherosclerosis.
- John L. VandeBerg, Ph.D., for equipment that will facilitate the isolation of DNA for the purpose of identifying genes that affect cardiovascular disease risk and determining whether individual baboons are cured of Chagas disease.

The Argyle stands as a symbol of progress toward a healthier tomorrow for the global community. OR MORE THAN 50 YEARS, THE ARGYLE, A HISTORIC SOUTHERN MANSION AND UNIQUE PRI-VATE CLUB, HAS BEEN DEVOTED EXCLUSIVELY TO THE SUPPORT OF THE LIFE-SAVING EFFORTS OF THE TEXAS BIOMEDICAL RESEARCH INSTITUTE. FOUNDED IN THE 1950S AND LOCATED ABOUT THREE AND A HALF MILES FROM DOWNTOWN SAN ANTONIO, THE 1,400-MEMBER CLUB SERVES AS A BOND BETWEEN ONE OF THE COUNTRY'S LEADING INDEPENDENT RESEARCH INSTITU-TIONS AND THOSE WHO GIVE TIME AND MONEY TO SUPPORT IT.

Originally built in 1854 as the headquarters of a horse ranch that extended from downtown San Antonio to the town of Boerne, some 30 miles distant, the mansion was an outpost of Texas hospitality. Through a succession of owners, it epitomized the pleasant ways and good living of the storied South. It was purchased in 1884 by two Scotsmen, who added the third floor and opened a hotel. They named it The Argyle because the surrounding rolling hills reminded them of their native Scotland. Happily, The Argyle came into the capable hands of the fabulous Miss Alice O'Grady around the turn of the century. She managed The Argyle and made it legendary for its fine table and illustrious guests.

In 1954, Dr. Harold Vagtborg, the Institute's first president, and Betty Slick Moorman, sister of founder Tom Slick Jr., discussed ways to interest more people in Texas Biomed's work and to create a broader and more permanent base of support for its research programs. Betty Moorman suggested the establishment of a high-caliber club whose members would make an annual contribution to Texas Biomed, and thus The Argyle of today was formed.

Restored in 1956, The Argyle stands as a symbol of progress toward a healthier tomorrow for the global community. Formed by persons deeply interested in the work of Texas Biomedical Research Institute, the club is a meeting place for men and women of science and civic leaders who have dedicated personal resources for the advancement of the Institute.

The Argyle is the scene of many grand occasions such as weddings and family events, as well as meetings of numerous Texas Biomed support groups and trustees. One of the most popular initiatives is a series of "Fireside Chats," held for Argyle members and guests. This program allows members to meet with Texas Biomed scientists and others in a social setting to enjoy an exchange of ideas and information regarding the scientists' research efforts. Argyle members enjoyed six of these "chats" in 2011. Members were treated to a talk in February by Anthony Comuzzie, Ph.D., on "Genetics, Obesity and Diabetes." In March, Andrew Hayhurst, Ph.D., provided a discussion on "Botox: Friend or Foe?" Kenneth P. Trevett, J.D., President, Texas Biomedical Research Institute, in April discussed the broad scope of the organization's reach with "Texas Biomed...A Local Dream ... An International Vision." Lorena M. Havill, Ph.D., kicked off the fall series with a talk titled "Can You Really Predict the Weather with Your Arthritic Knees?" In October, Robert Davey, Ph.D., gave a creative presentation on "Contagion: Can Your Allergy Pill Save Your Life?" The year was capped off in November by Laura Cox, Ph.D., who provided recent developments in genetics in a talk on "Genes. Maternal Nutrition and Heart Disease."

Argyle members continue to live up to their vision of honoring the past while at the same time changing the future through their philanthropic investments in Texas Biomed.



1854

year built as the headquarters of a horse ranch that extended from downtown San Antonio to Boerne

1884

year purchased by two Scotsmen who named the Argyle after the surrounding rolling hills that reminded them of their native Scotland

1956

year the Argyle was restored as a club for those dedicated to the advancement of the Institute

ADMINISTRATION

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 Chief Scientific Officer

 John L. VandeBerg, Ph.D.

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BACK COVER: This image shows smooth muscle cells derived from baboon embryonic stem cells. Alpha-actin-2, a cytoplasmic protein that is specific to smooth muscle cells, is stained green. The cell nuclei are stained blue.

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IMAGES AND ILLUSTRATIONS

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