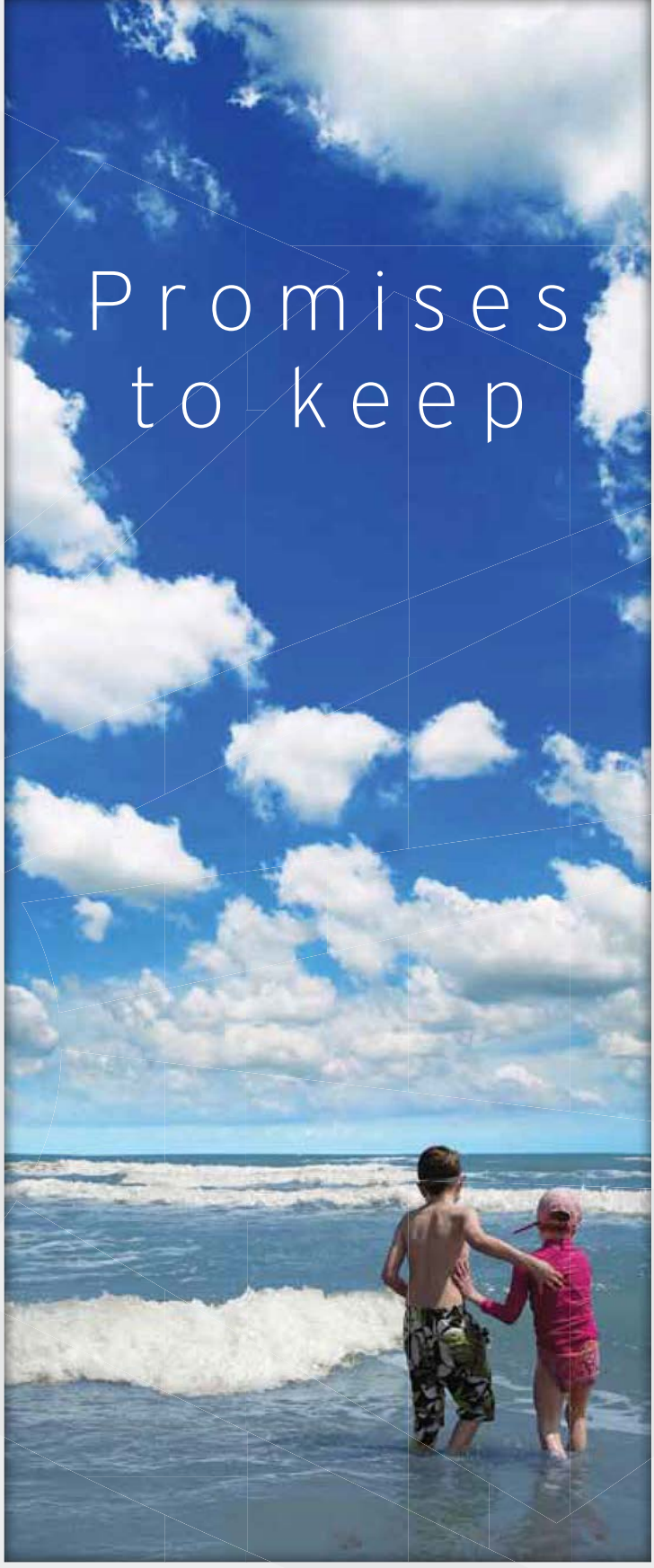
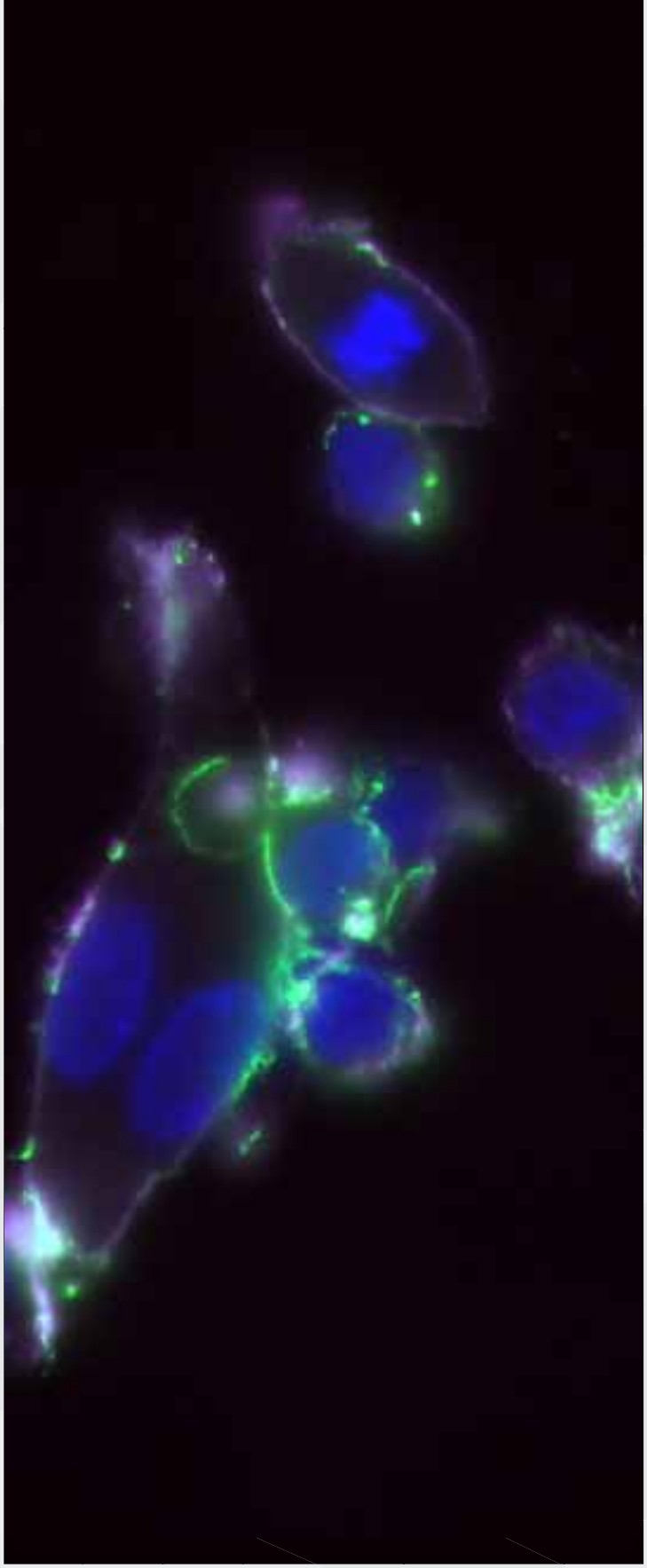
Promises to keep



Texas Biomedical Research Institute

2012 Annual Report



Promises to keep

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FRONT COVER, CONTENTS PAGE: *At the Department of Genetics 30th anniversary symposium, Kim Shepperd spoke eloquently about her family's efforts to accelerate the progress and promise of research to improve the lives of those with cystinosis, including her children, John Ben and Ava, shown on the cover and contents page. Texas Biomed scientists have identified the VNN1 gene which is involved in the biological pathway that is associated with cystinosis, a rare genetic disorder that causes the body's organs to eventually shut down if untreated. Continued research on the effects of this gene may lead to improved treatments for cystinosis patients. (See page 14.)*

FRONT INSIDE COVER: *Image shows endothelial progenitor cells derived from baboon embryonic stem cells. These cells possess two proteins that are characteristic of endothelial cells, CD31 (green) and CXCR4 (purple).*

ABOUT TEXAS BIOMED

The Institute is home to extraordinary resources that give its scientists and their collaborators an advantage in the search for discoveries to fight disease.

AS ONE OF THE WORLD'S LEADING INDEPENDENT BIOMEDICAL RESEARCH INSTITUTIONS, 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 81 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 and home to the world's largest baboon research colony, including a unique pedigreed baboon colony that is invaluable for genetic studies on complex diseases. The 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 4 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 have 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 disease-influencing 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.

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 heavily on philanthropy to maintain its excellence. Approximately 75 percent of the Institute's annual budget is funded from highly competitive, peer-reviewed federal research grants and contracts, while another 3 percent comes from commercial contracts with biotechnology and pharmaceutical firms. Philanthropy constitutes the second largest portion of the Institute's budget, as about one-fifth of Texas Biomed expenses are met by the generous contributions of foundations, corporations, and individuals, as well as income from Texas Biomed's endowment and mineral 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 the website at www.TxBiomed.org.

Enhancing lives through discovery℠

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

WWW.TXBIOMED.ORG

LETTER FROM THE PRESIDENT

IT IS AN INTERESTING CHARACTERISTIC OF THE HUMAN PSYCHE TO LOOK BEYOND OUR IMMEDIATE BOUNDARIES IN ORDER TO SEARCH FOR EXCELLENCE. YOU ARE FAMILIAR WITH THE COMMON EXPRESSION, "THE GRASS IS ALWAYS GREENER ON THE OTHER SIDE OF THE FENCE."

But in San Antonio, our biomedical research organizations are not simply good at what they do, they are world leaders. And the quality of their work is made even more outstanding by their willingness to work together, in synergistic fashion, to solve problems that quite literally plague our society. I am proud to say that one of these leading institutions, and the first and largest of its kind in San Antonio *and* the State of Texas, is the Texas Biomedical Research Institute.

Since its founding in 1941, Texas Biomed has had an outsized impact on science, and derivatively, on medical care throughout the world. Whether we cite the invention of the high frequency ventilator, which has saved hundreds of thousands of premature infants, the development of a vaccine against hepatitis B, the creation of SOLAR, software that has greatly enhanced human genetic analysis, or the identification of the strain of anthrax that killed or injured numerous people in the bio-terror attacks of 2001, Texas Biomed has played a critical role in improving public health.

This is just as true today when our scientists are examining new vaccine strategies against a variety of pathogens; when we are continually identifying inheritable influences on human diseases such as cardiovascular illness, diabetes, arthritis, macular degeneration, schizophrenia and depression; and when we are developing new models of disease which can accelerate the search for better therapies and even cures. This is the promise of our work…and our promise to you.

We are preparing for the future…because our efforts really matter. In May, we broke ground for a 70,000-square-foot laboratory and scientific support building that will be completed and occupied by early 2014. This facility will significantly increase our research capacity. We have been aggressively recruiting new faculty members in Genetics, Virology/Immunology and the Southwest National Primate Research Center to increase our capability of translating discoveries into lead technologies for patient care. We have spearheaded the effort to form a joint vaccine center in San Antonio to accelerate the search for new preventative approaches to disease, and we are participating in a trans-Texas initiative to promote vaccine research and development.

All these initiatives, and more, have been facilitated by our Board of Trustees and community volunteers who know the power of biomedical research and what it can do to improve and save lives. We are extremely grateful to these and to many other individuals who give of themselves and their resources so that we can better pursue our mission.

Excellence in what we do is an ongoing pursuit…and an ongoing responsibility…for we have promises to keep.

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

"EXCELLENCE IN WHAT WE DO IS AN *ongoing pursuit...* AND AN *ongoing responsibility...* FOR WE HAVE PROMISES TO KEEP."

– KENNETH P. TREVETT,
PRESIDENT AND CEO

LETTER FROM THE CHIEF SCIENTIFIC OFFICER

"THE TEXAS BIOMEDICAL RESEARCH INSTITUTE WILL MARKEDLY STRENGTHEN ITS CAPACITY TO HARNESS THE *energy of its creative scientists* BECAUSE YOU ARE PARTNERING TO *improve lives worldwide.*"

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

2012

SCIENTISTS AT THE TEXAS BIOMEDICAL RESEARCH INSTITUTE WROTE ANOTHER CHAPTER IN THE IMPRESSIVE HISTORY OF OUTSTANDING PRODUCTIVITY AND CREATIVITY IN 2012. UTILIZING RARE RESEARCH RESOURCES THAT, IN COMBINATION, PROVIDE A UNIQUE SCIENTIFIC EDGE, THEY MADE MAJOR ADVANCES THAT CONTRIBUTED TO THE INSTITUTION'S MISSION OF IMPROVING THE HEALTH OF OUR GLOBAL COMMUNITY.

During 2012, Texas Biomed researchers published well over 100 manuscripts in the national and international scientific literature. Each of these peer-reviewed articles is a measurable step forward in our quest to understand human biology and the origins and development of diseases. They include —

- Demonstrating that two off-the-shelf cancer drugs blocked the deadly Ebola virus from reproducing in the test tube — an early, promising advance against a disease and potential biological weapon with no approved treatments or vaccines (*Science Translational Medicine* 4, 123ra24 2012). These drugs could be used to fight a surprising variety of diseases – including both smallpox and tuberculosis – by shutting down human enzymes that some bacteria and viruses exploit, and which are dysregulated in certain cancers.
- Finding that the emergence of resistance to the drug artemisinin in western Thailand has created a critical impediment in global efforts to control and eliminate malaria worldwide (*The Lancet* Volume 379, Issue 9830, Pages 1960 - 1966, 26 May 2012 doi:10.1016 S0140-6736(12)60484). A second study by the same research group identified a major region of the malaria parasite genome associated with artemisinin resistance, raising hope that there will soon be effective molecular markers for monitoring the spread of resistance (*Science*, 2012; 336 (6077): 79).
- Identifying variants in several genes that are responsible for causing susceptibility to obesity among Hispanic children. (*PLOS ONE* 7(12): e51954). Characterization of these variants will enable an understanding of their mechanisms of action and the development of strategies aimed at curbing the epidemic of childhood obesity.
- Establishing that a monoclonal antibody tested in the chimpanzee model prevents infection by the hepatitis C virus (*PLOS Pathogens* 8(8): e1002895 doi:10.1371/journal.ppat.1002895). This potential treatment may eventually prove to be effective for patients with end-stage liver disease undergoing liver transplantation as a result of hepatitis C virus infection.
- Developing a faster, less expensive route to screen potential tests for bioterror threats and accelerate the application of countermeasures (Nature Publishing's *Scientific Reports* 2, Article number: 807 doi:10.1038/srep00807). The new process screens for pairs of affinity reagents – molecular magnets that bind and hold on to their targets, be they toxins, viruses or bacteria. That will enable countermeasures to be selected and utilized much faster than is the current practice.
- Demonstrating that cells derived from embryonic stem cells can repair damaged blood vessels taken from baboons (*Stem Cells Dev.* 2012 Oct 10. [Epub ahead of print] PMID: 22931470). The study showed that an artery stripped of its inner cells, and then repaired through the use of stem cells, had completely normal function and could do everything that a normal artery does in a healthy individual.

During 2012, Texas Biomed scientists were awarded $41.9 million in grant and contract funding. Twelve new multiyear grants in excess of $1 million were awarded. This level of success in the current difficult funding environment attests to the high level of proficiency and competitiveness of our scientists.

Finally, I must express our profound appreciation to donors who provided 100 percent of the funding for our new 70,000-square-foot building, which will house 15 new laboratories. The Texas Biomedical Research Institute will markedly strengthen its capacity to harness the energy of its creative scientists because you are partnering to improve lives worldwide.

Sincerely,

John L VandeBerg

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

CAMPUS DEVELOPMENT

LATE IN 2012, THE FIRST EXTERIOR WALLS OF TEXAS BIOMED'S NEW 70,000-SQUARE-FOOT LABORATORY AND OFFICE COMPLEX WERE PUT IN PLACE. THIS MAJOR MILESTONE CAME AFTER MONTHS OF GROUND PREPARATION FOLLOWING THE MAY GROUNDBREAKING. NAMED THE EARL SLICK RESEARCH CENTER AFTER THE BROTHER OF TEXAS BIOMED FOUNDER TOM SLICK, THE $26.5 MILLION FACILITY IS PART OF A CAMPUS MASTER PLAN THAT INCLUDES A MAJOR EFFORT TO RECRUIT MORE WORLD-CLASS SCIENTISTS, ENHANCE EXISTING RESEARCH PROGRAMS, AND INITIATE NEW ONES TO ACCELERATE THE PACE OF SCIENTIFIC DISCOVERY. THE BUILDING WILL CONTAIN 15 NEW RESEARCH LABORATORIES.

Having raised some $32 million in gifts, Texas Biomed also announced the public phase of a capital campaign and now plans to raise another $10 million during 2013 and 2014.

A total of 10 new researchers will be recruited to grow and advance Texas Biomed's pacesetting programs. The goal of these recruitments will be to promote the translation of discoveries into medical applications. The designers of the building are Lake Flato Architects of San Antonio and FKP Architects of Houston. The builder is Vaughn Construction.

1. FACILITIES COMMITTEE: Facilities Committee members meet with architect Ted Flato. From left to right are Walter Embry, Rex Amini, Ted Flato of Lake Flato Architects, J.R. Hurd, Abigail G. Kampmann and Curtis V. Anastasio.

2. GROUNDBREAKING: Phyllis Slick Cowell, the daughter of Earl Slick, and members of her family attended the groundbreaking on May 24. From left to right are Maile Cowell, Jane Ives, Michelle Cowell, Allen Ives, Lynn Ives, John Cowell and Phyllis Slick Cowell.

3. CAMPAIGN CO-CHAIRS: From left to right, campaign co-chair Ronald K. Calgaard, Ph.D.; Corbett Christie, Texas Biomed Vice President for Institutional Advancement; campaign co-chair John C. Kerr; and Kenneth P. Trevett, Texas Biomed President and CEO.

FIRST WALLS: The first walls of the Earl Slick Research Center were put into place on December 26, 2012.


2


3

FEATURE

1982 -

Texas Biomed's Department of Genetics Celebrates 30 Years

IN DECEMBER OF 1979, A YOUNG GENETICIST AT THE UNIVERSITY OF WISCONSIN RECEIVED A PHONE CALL FROM HENRY MCGILL, M.D., A CARDIOVASCULAR DISEASE RESEARCHER FROM A LITTLE-KNOWN BIOMEDICAL RESEARCH FACILITY IN TEXAS. MCGILL ASKED JOHN L. VANDEBERG, PH.D., IF HE WAS INTERESTED IN INVESTIGATING THE LINKS BETWEEN DIET AND HEART DISEASE. AFTER DISCUSSING AN OFFER WITH HIS COLLEAGUES, VANDEBERG LATER RECALLED BEING TOLD THAT NOBODY HAD HEARD OF THE PLACE AND THAT IF HE TOOK THE JOB, "I WOULD AMOUNT TO NOTHING AND NOBODY WOULD EVER HEAR OF ME AGAIN."

DEPARTMENT OF GENETICS MILESTONES:

1982 The Department of Genetics is established by John L. VandeBerg.

The Genetic Analysis Workshop is founded by Texas Biomed scientist Jean MacCluer.

The Baboon Program Project is initiated to study risk factors for cardiovascular disease in a nonhuman primate model.

2012

However, VandeBerg's instincts told him to accept the job. And since then he has amounted to plenty, and has been heard of ever since. And what was the Southwest Foundation for Research and Education in 1979, is now the Texas Biomedical Research Institute and is recognized as a world leader in research on the genetics of complex diseases.

EARLY YEARS

With an initial staff that included a postdoctoral fellow, a technician and a secretary, VandeBerg began recruiting faculty to join the genetics program shortly after his arrival. His first two faculty hires were Jean MacCluer, Ph.D., and Bennett Dyke, Ph.D., who added expertise in population genetics and computational approaches to VandeBerg's strengths in biochemical genetics. By January of 1982, just 16 months after VandeBerg started work at the Southwest Foundation, the genetics program had grown to three scientists, eight technicians, a secretary and two postdoctoral fellows. At this point, the program was judged to be of sufficient size and strength to gain departmental status. By 2012, the number of staff had grown to 111, with 15 faculty members; 14 postdoctoral fellows; 57 technical staff and 5 administrative staff.

The Department celebrated its 30th anniversary at a symposium held on December 7 on the Texas Biomed campus. The symposium featured a series of presentations including a review of the history of the Department, descriptions of current programs, and discussions of the international impact of the Department's training and research.

The initial focus of the Department's research efforts was on heart disease in the baboon model. Researchers in the Department of Genetics participated in a multidisciplinary study assessing the role of genes and dietary factors on risk factors for heart disease in baboons. This work was first funded in 1982 by NIH as a program project entitled Diet, Stress, and Genotype in Primate Atherosclerosis. Known as the Baboon Program Project, this research effort led to the development of the vast majority of the research programs active in the Department today.

Building upon the findings of the research on risk factors for atherosclerosis in baboons, MacCluer established the San Antonio Family Heart Study (SAFHS) as a program project in 1991. This project involved studying 1,400 members of 40 Mexican-American families and led to recognition of the Department as a leader in research on minority health. Participation in other studies focused on minority populations followed, including the Strong Heart Study of heart disease in Native Americans living in the Dakotas, Arizona and Oklahoma; the Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) study looking at risk for heart disease in Eskimos; and the Zuni Project, which assessed the genetic components of kidney disease in a Zuni population from New Mexico. All of these major programs on heart disease remain active today and depend on the Department's state of the art genotyping capabilities and unparalleled computing resources.

Key to the Department's success are its resources and innovative thinking, noted Eric Moses, Ph.D., formerly of Texas Biomed, and now at the University of Western Australia in Perth. Department members helped him to expand his work on preeclampsia, a common complication of human pregnancy. Of his nearly seven years in San Antonio, Moses said: "The supportive culture permitted bold science, all made possible by good people," a sentiment echoed by several speakers who recounted their training and work at Texas Biomed.

1991 The San Antonio Family Heart Study begins to study genetic components of risk for heart disease in Mexican Americans.

1995 The Jiri Helminth Project is established to study one of the largest documented human pedigrees available for genetic research.

SOLAR, a genetic analysis software package developed by Texas Biomed scientists and now used by over 5,000 researchers worldwide, is released.

MAJOR RESEARCH AREAS

The senior faculty in the Department of Genetics gave presentations on the major areas of research currently being conducted in the Department.

DIET AND GENOTYPE IN PRIMATE ATHEROSCLEROSIS

Growing out of earlier work by McGill and his colleagues conducted in the 1960s and 1970s, the Baboon Program Project has been funded continuously for 30 years, noted Anthony Comuzzie, Ph.D. The project has enabled Texas Biomed scientists to develop the most comprehensive genetically and phenotypically characterized pedigree of nonhuman primates currently available for research on the genetics of complex diseases. The project also set the stage for the focus on large family based studies, which has become a hallmark of work done in the Department. Project scientists have identified a number of genes involved in mediating a variety of risk factors for cardiovascular disease, hypertension, obesity, and diabetes. The wealth of data available for seven generations of baboons makes the colony invaluable for genetic research on the determinants of variation in both normal and disease-related traits.

GENETICS METHODS

Exploiting extended complex pedigrees such as those in the Baboon Program Project requires specialized analytical approaches. For three decades, the Genetics Analysis Workshop (GAW) has provided a testing ground for novel genetic methods. GAW has grown dramatically since it was established by MacCluer in 1982, said current director Laura Almasy, Ph.D. The 18th workshop, focusing on methods to analyze comprehensive sequence data now being generated for human studies, was held in October 2012 in Stevenson, WA, and attracted 182 scientists. Since its inception, GAW has had more than 2,800 registrants, with many 'regulars' who have attended multiple workshops.

Almasy described PEDSYS, a database system developed by Dyke as a specialized tool for management of genetic, pedigree and demographic data. It was designed to support genetic analyses of complex extended pedigrees of either human or animal subjects.

Almasy also outlined how statistical geneticists at Texas Biomed, led by John Blangero, Ph.D., developed the program SOLAR to implement state-of-the-science genetic analysis approaches that were first tested at the Genetic Analysis Workshop. Introduced in 1998, SOLAR is an extensive, flexible software package for variance component analysis, including linkage analysis, and quantitative genetic analysis. It recently has been expanded to include novel methods for high-throughput analysis of high dimensional genomic data. The software is now used by over 5,000 genetics researchers worldwide.

SAN ANTONIO FAMILY HEART STUDY

John Blangero, the current director of the SAFHS, described the project's overall aim of identifying genes influencing risk for cardiovascular and other complex diseases, and the importance of large pedigrees for studying the rare variants responsible for these disorders. The SAFHS has employed advanced genetic approaches

From left to right: At 30th anniversary symposium, Department of Genetics founder John L. VandeBerg, Ph.D., and first scientist hires Jean MacCluer, Ph.D., and Bennett Dyke, Ph.D.

DEPARTMENT OF GENETICS MILESTONES:

1997 Texas Biomed geneticists discover the first human quantitative trait locus for leptin levels in the San Antonio Family Heart Study, a finding which led to the identification of the POMC gene as playing a critical role in obesity.

1998 Publication of the landmark paper "Multipoint quantitative-trait linkage analysis in general pedigrees" by Laura Almasy and John Blangero, the most cited article in the history of Texas Biomed with over 2,000 citations.

1999 The National Institutes of Health establishes the Southwest National Primate Research Center on the Texas Biomed campus with John VandeBerg as Director.

to generate data on about 3,300 individuals in order to find disease-related genes. The study recently embarked on whole genome sequencing of the DNA of study participants to comprehensively identify all disease-related variation. Blangero noted that the SAFHS investigators have initiated a collaboration with a major pharmaceutical company to identify therapeutic targets for cardiovascular disease. New areas of investigation with SAFHS participants include planned projects on bone, eye and sleep-related diseases.

DIABETES AND OBESITY RESEARCH

The Department's work on diabetes and obesity grew out of the recognition of high rates of these diseases in the Mexican-American population that was the focus of the SAFHS. Ravindranath Duggirala, Ph.D., an internationally recognized leader in diabetes research, noted that Texas Biomed geneticists have been in the forefront of genomics research related to diabetes, obesity, and related diseases, both in adults and children. Texas Biomed participates in an international consortium of diabetes studies that aims to identify rare variants influencing diabetes and related traits. As part of this collaborative effort, the Mexican-American family samples from the SAFHS and the San Antonio Family Diabetes Study have been used to generate the whole genome sequence data for more than 1,000 individuals to facilitate more intensive studies of diabetes. Also, the high-density fine-mapping of previously identified gallbladder disease susceptibility loci has resulted in finding novel genetic regions that influence the disorder. The ultimate goal of the Department's research on diabetes and related disorders is to develop lifestyle and therapeutic interventions to prevent or cure these debilitating chronic diseases.

OSTEOPOROSIS AND BONE BIOLOGY

Texas Biomed studies of bone genetics began during the 1990s, noted Michael Mahaney, Ph.D. For much of that time, Texas Biomed geneticists focused on osteoporosis, primarily using pedigreed baboons because of their genetic and physical similarities to our own species. In recent years, bone genetics research has expanded significantly. Geneticists now conduct studies with both human and nonhuman primate groups, taking advantage of unique genetic and genomic resources developed at Texas Biomed. Recent, highly innovative work by the department's Lorena Havill, Ph.D., showing that baboons also suffer from osteoporosis and osteoarthritis, has opened the doors to new ways to study and possibly treat these disorders in humans. Mahaney himself leads a study of the genetic determinants of bone-related traits in the Jirel population of eastern Nepal that is also improving our understanding of the factors underlying risk for osteoporosis.

"IN THE FUTURE, WE'LL HAVE WHOLE GENOME SEQUENCE INFORMATION FOR ALL OUR STUDY POPULATIONS, INCLUDING THE NONHUMAN PRIMATE POPULATIONS. *With this wealth of information, we will be able to make rapid progress* IN DISCOVERING FUNCTIONAL VARIANTS AND THE CAUSAL GENES UNDERLYING DISEASE."

— SARAH WILLIAMS-BLANGERO, PH.D.

INFECTIOUS DISEASE GENETICS

The parasitic diseases represented in the Department's portfolio – ascariasis, schistosomiasis, *Trypanosoma cruzi* infection, and malaria – are jointly responsible for almost a million deaths annually, and cause severe morbidity in millions more. Tim Anderson, Ph.D., described the disturbing spread of resistance to the antimalarial drug artemisinin in Southeast Asia, and detailed how his research team has identified a major region of the malaria parasite genome associated with resistance, raising hope that there will soon be effective molecular markers for monitoring resistance spread. Switching parasites, he described the development of a genomic map for the blood fluke Schistosoma mansoni, the cause of schistosomiasis. In collaboration with Phillip LoVerde, Ph.D., of the UT Health Science Center San Antonio, Anderson's team has successfully exploited the genomic map and genome

Sarah Williams-Blangero becomes Chair of the Department of Genetics.

Texas Biomed geneticists publish the baboon gene map, the first genetic linkage map of a nonhuman primate species.

2003 The AT&T Genomics Computing Center is established with 1,000 processors, making it the largest computer cluster in the world dedicated to human genetic analysis.

Shepperd's two children, John Ben and Ava, suffer from cystinosis, a rare, genetic disorder that causes the body's organs to eventually shut down if untreated.

sequence to incriminate a single mutation underlying resistance to the drug oxamniquine.

UNIQUE POPULATIONS

Department Chair Sarah Williams-Blangero, Ph.D., described the unique pedigrees that Texas Biomed scientists have documented in populations across the world. These extended families are among the largest pedigrees available to genetic researchers and provide Texas Biomed scientists with unique opportunities to assess the genetic components of a broad range of diseases. As described by Williams-Blangero, in many areas of the world, the presence of large, stable populations makes it possible to assess huge numbers of relatives who live within a fairly small geographic region. She described the process and some occupational hazards of conducting research with these populations ranging from work on Chagas disease in Brazil, to studies of heart disease in Alaska Natives, to research on worm infections in the Jirels of Nepal. These studies produce valuable genetic data and provide important opportunities for studying the effects of genes on disease risk. Because these international studies of extended families involve regular medical care for these populations, they also are a tribute to Texas Biomed's mission "to improve the health of our global community."

A FAMILY'S STORY

The final talk of the symposium was a moving presentation by Kim Shepperd, who highlighted the direct impact of research conducted by Texas Biomed geneticists on our local community. Her two children, John Ben and Ava, suffer from cystinosis, a rare, genetic disorder that causes the body's organs to eventually shut down if untreated. She recounted her family's struggle with the disease and their search for better therapies.

Henry McGill, M.D., a cardiovascular disease researcher, asked John L. VandeBerg, Ph.D., if he was interested in investigating the links between diet and heart disease.

Seeking to find a new innovative way to help families struggling with this disease, Kim and her parents Richard and Dianne Azar, sat down with Texas Biomed scientists to discuss developing a research program that could pave the way to new treatments and possibly a cure. Using the resources of the SAFHS, John Blangero proposed a bold plan of genetic sleuthing, in which Texas Biomed scientists would examine the relationship of all the genes in the human genome to the CTNS gene which goes awry in cystinosis.

So far, this research, which was funded by the Azar family, has resulted in the identification of a gene called VNN1 which is involved in the biological pathway that is associated with cystinosis. The gene also has implications for heart disease, particularly for high density lipoprotein cholesterol which plays a protective role in cardiovascular disease. Continued research on the effects of this gene ultimately may result in new preventions and treatments for a variety of disorders, and improve treatments for cystinosis patients. Richard Azar noted that "Dr. Blangero's grand idea appealed to me – and the success we have achieved to this point is just a beginning. Without risk, we never test the limits and challenge the unknowns. This may sound odd to some of you, but to someone in the oil and gas industry, it makes perfect sense."

In closing, Shepperd said: "We take it a day at a time at my house. We have so much admiration for our kids; they amaze us with their brave spirits every day. It's hard not to feel blessed."

The powerful new gene discovery methods used by Texas Biomed scientists to study cystinosis are already being applied to the search for genes that influence a wide variety of health problems. The rapid rate of progress means that many more important genetic discoveries are well within scientists' reach.

DEPARTMENT OF GENETICS MILESTONES:

2005 Texas Biomed geneticists discover the SELS gene as a novel player in human inflammation.

2006 Texas Biomed geneticists publish the rhesus monkey genetic linkage map.

2007 The Earl Slick Center opens to house Department of Genetics' offices and laboratories.

LOOKING TO THE FUTURE

As the Department continues to push the boundaries of the field, the future for patients everywhere will be altered for the better.

"In the future, we'll have whole genome sequence information for all our study populations, including the nonhuman primate populations. With this wealth of information, we will be able to make rapid progress in discovering functional variants and the causal genes underlying disease," Williams-Blangero said.

"As we move forward into this new era of genetics, more of our work will become biological as we seek to understand gene function and the mechanisms underlying how these genes work. This research effort will include high-throughput functional assays and studies of regulatory mechanisms such as whole genome methylation," she added.

The rapid refocusing of the field of human complex disease genetics on rare variation puts the Texas Biomed Department of Genetics in an exceptionally strong position. The focus on large extended pedigrees for over three decades and access to the unique populations is a huge advantage. "As the current generation of human geneticists is having to learn or relearn how to collect and work with pedigree information, we are at the cutting edge in generating and handling this type of data," Williams-Blangero noted.

Once scientists have complete genetic information, the battle will turn toward finding the best possible phenotypes that are related to the diseases under study. Soon a combination of genetics and environmental influences will be the gold standard for devising new ways to approach disease. The era of personalized medicine will have begun.

This again confirms that VandeBerg's hunch 30 years ago to accept the challenges awaiting him in Texas was spot on. ■

2012 RESEARCH

Texas Biomed Scientists Regenerate Damaged Artery

SCIENTISTS AT THE TEXAS BIOMEDICAL RESEARCH INSTITUTE HAVE DERIVED CELLS FROM BABOON EMBRYONIC STEM CELLS THAT CAN COMPLETELY REGENERATE THE INTERIOR SURFACE OF AN EXPERIMENTALLY DAMAGED ARTERY.

"THIS IS PROOF OF THE POTENTIAL FOR HARNESSING STEM CELLS TO *treat serious arterial disease.*"

— JOHN L. VANDEBERG, PH.D.

These early results show promise for eventually developing embryonic stem cell therapies to restore tissues and organs damaged by age or disease. Scientists even hope to heal brains that have begun to degenerate as a consequence of Parkinson's or Alzheimer's disease.

"Dr. Qiang Shi first cultured these stem cells in petri dishes under special conditions to make them differentiate into cells that are the precursors of blood vessels, and he saw that he could get them to form tubular and branching structures, similar to blood vessels," said John L. VandeBerg, Ph.D., Texas Biomed's chief scientific officer.

This initial finding gave Shi and VandeBerg the confidence to do complex experiments to find out if these cells could actually heal a damaged artery. The research was funded by the National Institutes of Health, the Voelcker Foundation and Texas Biomed's Founder's Council and was published in the journal *Stem Cells and Development*.

The scientists found that cells derived from embryonic stem cells could fully repair damaged arteries of baboons and "are promising therapeutic agents for repairing damaged vasculature of people," VandeBerg said.

Texas Biomed geneticists undertake and publish the world's first large-scale study using genome-wide transcriptional profiling, leading to the identification of the VNN1 gene as a potent mediator of HDL cholesterol.

2009 Publication of the third edition of "The Baboon in Biomedical Research."

2011 The AT&T Genomics Computing Center expands to 8,000 processors, dramatically increasing the speed of gene discovery. {X8}

THE RESEARCH PROCESS

The researchers first designed and custom-built a device meant for cultivating a living artery outside the body. They then connected a segment of a healthy baboon artery to plastic tubing and put it inside the device. The scientists then pumped fluid through the artery under pressure as if blood were flowing through it, while bathing the outside of the artery in another fluid. The entire system is called a bioreactor.

When the bioreactor conditions were perfected, the researchers completely destroyed the inner surface of a segment of artery. They then put cells derived from embryonic stem cells inside the artery to determine if these new cells could heal the inside of an artery that had been stripped of all the cells that line its surface. These new cells are called angioblasts — or prevascular cells — and they differentiate into endothelial cells that line the inside of the arteries and are responsible for normal arterial function.

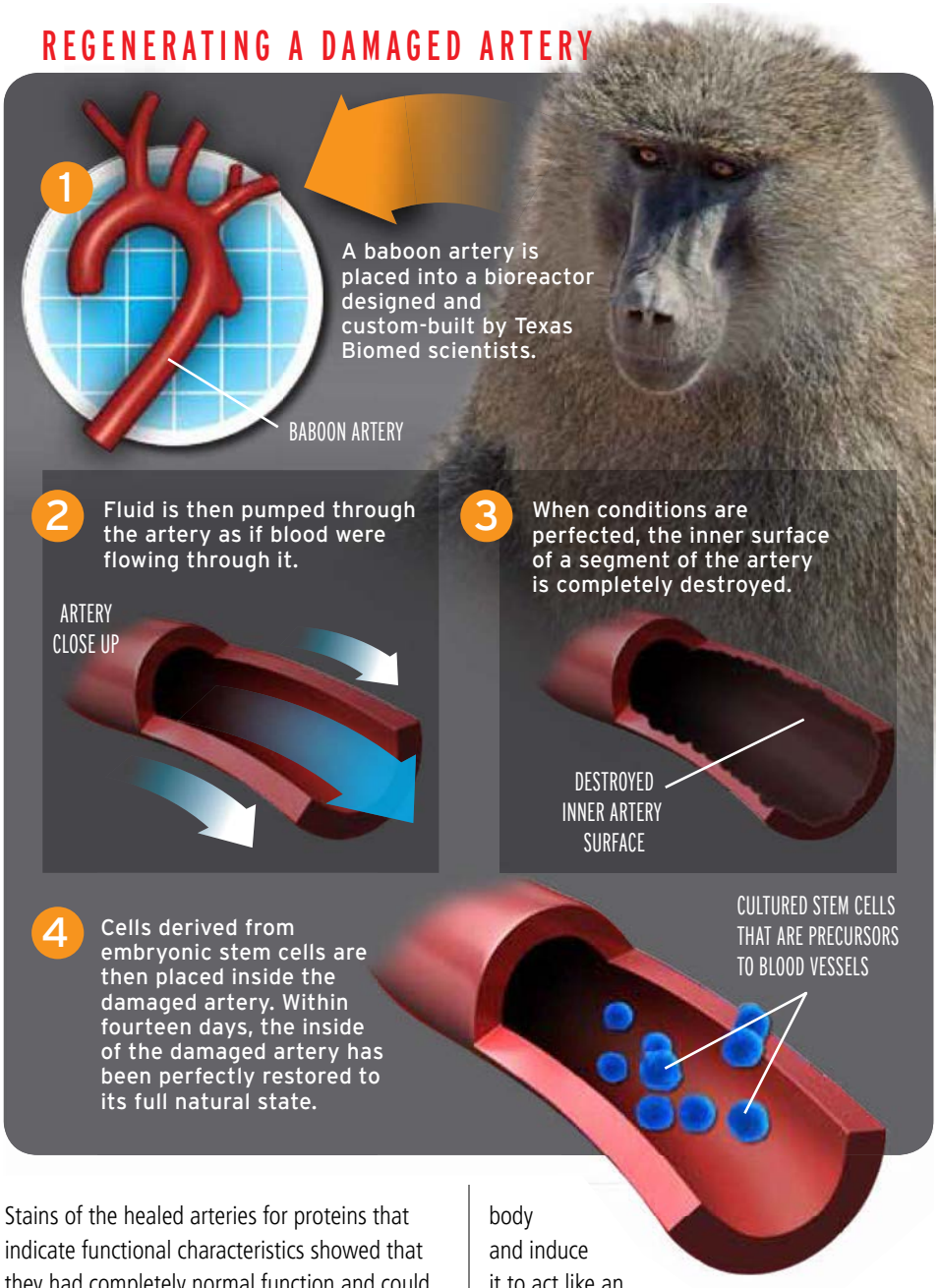
The scientists then connected the artery segment to the tubing in the bioreactor. Three days later, they saw that the complex structure of the inner arterial surface was beginning to regenerate. And by 14 days, the inside of the artery had been perfectly restored to its full natural state. It went from a nonfunctional tube to a fully functional complex artery.

EXTRAORDINARY IMPLICATIONS

"Just think of what this kind of treatment could mean to a patient who was suffering from progressive arterial disease," VandeBerg said. "This is the meaning of stem cell regenerative medicine — that is, a treatment with stem cells to regenerate a damaged or destroyed tissue or organ."

To show that the artery could not heal itself in the absence of stem cells, the scientists stripped a control artery of cells, but did not seed it with stem cells, and put it in the bioreactor. Fourteen days later, nothing had changed; no healing had occurred.

REGENERATING A DAMAGED ARTERY



Stains of the healed arteries for proteins that indicate functional characteristics showed that they had completely normal function and could perform everything that normal healthy arteries do in a healthy individual.

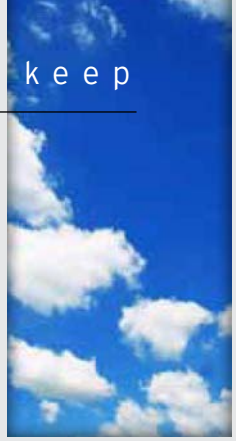
"This is proof of the potential for harnessing stem cells to treat serious arterial disease," said VandeBerg.

Eventually, scientists hope to be able to take a skin cell or a cell from any other tissue in the body and induce it to act like an embryonic stem cell in its capacity to differentiate into any tissue or organ. One vision of the future, for example, is taking skin cells from patients who have a damaged pancreas due to diabetes, inducing them to become stem cells, and then growing a new, normal pancreas. ▪

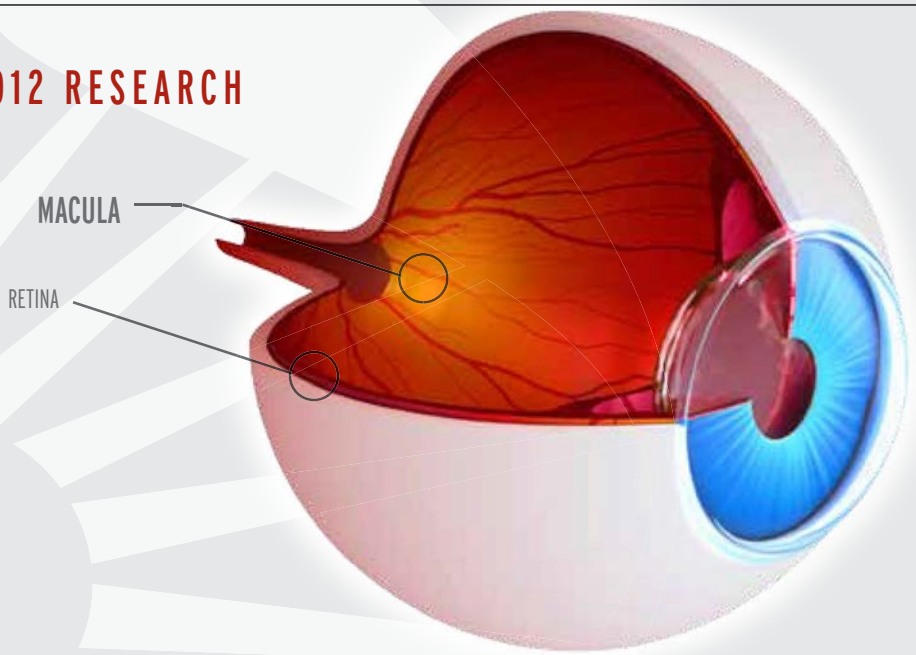
DEPARTMENT OF GENETICS MILESTONES:

2012 Texas Biomed Geneticists discover a major genome region underlying artemisinin resistance in malaria.

First large-scale study of whole genome sequencing in extended human pedigrees as part of the T2D-GENES Consortium.



2012 RESEARCH



New Study Focuses on Macular Degeneration, a Widespread Vision Disorder in Elderly

IF YOU HAVE A GRANDPARENT OR RELATIVE WHO IS OLDER THAN 65, HE OR SHE HAS A 30 PERCENT CHANCE OF SUFFERING FROM AGE-RELATED MACULAR DEGENERATION, A POTENTIALLY BLINDING AND LIFE-CHANGING EYE CONDITION. FOR INSTANCE, THE DISORDER PREVENTS MANY SENIORS FROM DRIVING AUTOMOBILES.

"MACULAR DEGENERATION COULD BE TERMED A *poster child* FOR COMMON COMPLEX DISEASES."

— MATTHEW JOHNSON, PH.D.

Age-related macular degeneration (AMD) is common in those older than 50 years of age and is a leading cause of vision loss in older adults. It gradually destroys the eye's macula, an area of the retina that provides the sharp, central vision needed for seeing objects clearly. Common symptoms are blurring of print, a dark or black spot in the center of vision, or distorted straight lines. A family history and environmental factors like smoking are known to increase the risk for AMD.

Now, with a new $2.93 million grant from the National Institutes of Health, scientists at Texas Biomed have teamed up with researchers at the Casey Eye Institute (CEI), led by Michael Klein, M.D., at the Oregon Health and Science University in Portland. The team plans to hone in on novel AMD genetic risk factors with the goal of developing new treatments. Research on the project began during the summer of 2012 and is scheduled to last four years.

The new AMD study will involve 1,400 individuals from 150 families who have been identified by Klein at CEI. The research will focus on identifying new genetic variations using the powerful DNA sequencing instruments housed at Texas Biomed. While some genetic variations associated with AMD have already been identified by other scientists, the research team on the new grant hypothesizes that remaining genetic risk factors of AMD are due to less common, but functionally significant, gene variations.

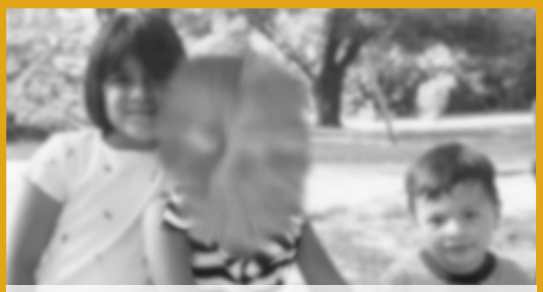
GENE VARIANTS AND DISEASE

"Macular degeneration could be termed a poster child for common complex diseases," said Matthew Johnson, Ph.D., a Texas Biomed geneticist and principal investigator of the Texas Biomed subcontract on the grant. "A small number of genetic variants, about five, account for approximately 50 percent of variation we see in individuals with AMD. This is compared with type 2 diabetes, for example, where about 18 genetic variants account for as little as 6 percent of the variation we see in individuals with this condition."

"This is an exciting new area of research for us," said Genetics Department Chair Sarah Williams-Blangero, Ph.D. "Matt's work on genetic determinants of ocular

FACTS ABOUT AGE-RELATED MACULAR DEGENERATION

Age-related macular degeneration (AMD) is a potentially blinding and life-changing eye condition. It gradually destroys the eye's macula, which provides the sharp, central vision needed for activities such as reading, face recognition, and driving a car.



HOW THINGS LOOK WITH AMD

If you have a grandparent or relative who is more than 65 years old, he or she has a 30 percent chance of suffering from age-related macular degeneration.

1/2

A small number of genetic variants, about five, account for approximately 50 percent of variation we see in individuals with AMD.

AMD is common in those older than 50 years of age and is a leading cause of vision loss in older adults.

Studies found that patients at risk for developing an advanced form of AMD lowered their risk by about 25 percent when treated with a high-dose combination of vitamin C, vitamin E, beta-carotene, and zinc.

The new AMD study will involve 1,400 individuals from 150 families who have been identified by researchers at the Casey Eye Institute.

AMD is predicted to increase by more than 50 percent by the year 2020, substantially increasing the societal health burden.

disease will generate important novel findings and also will lay the groundwork for expanding research on eye-related traits in our other human population studies."

Johnson has vast experience working on the identification of genes that underlie or contribute to the onset and severity of important medical conditions, including preeclampsia, a dangerous human pregnancy disorder. Preeclampsia occurs in approximately 4 percent of first-time pregnancies, where the expectant mother develops high blood pressure and elevated levels of protein in her urine (which may indicate kidney damage) during pregnancy. Preeclampsia and AMD are extremely complex, involving multiple genes and, most likely, multiple nongenetic insults. Furthermore, it is quite likely that each of these disorders has several variations, making the search for treatments and cures all the more complex.

At the 2012 meeting of the International Society for the Study of Hypertension in Pregnancy in Geneva, Switzerland, Johnson received the Zuspan Award for outstanding basic science work in relation to the study of hypertension in pregnancy. In recognition of his work, he also received a 40-under-40 award during 2012 from the *San Antonio Business Journal*. Each year, the newspaper selects 40 exceptional individuals under the age of 40 who are making great strides in their professional careers and are contributing positively to the San Antonio community. The winners were selected from a pool of more than 200 nominations.

SYMPTOMS AND TREATMENTS

Macular degeneration occurs in dry and wet forms. Most people have the dry form, which is instigated by the breakdown of light-sensitive cells in the macula. A hallmark feature of dry AMD is the appearance of drusen, which are yellow or white fatty deposits under the retina. These changes result in gradual vision loss. In the wet form, new blood vessels beneath the retina leak fluid or blood and usually cause a rapid decline in vision if left untreated.

Treatment for macular degeneration varies, depending on the type and severity of the disease. Nutritional supplements may help reduce the impact of AMD in some people. A large scientific study found that patients at risk for developing an advanced form of AMD lowered their risk by about 25 percent when treated with a high-dose combination of vitamin C, vitamin E, beta-carotene, and zinc. However, these supplements did not benefit those with less advanced forms of AMD. Hence, additional treatments are necessary to halt the progression of this disorder.

Some 1.75 million people in the United States suffer from the advanced, visually disabling form of AMD. More than 7 million additional individuals have earlier retinal changes placing them at high risk of developing advanced AMD. In those older than 75 years, the prevalence of advanced disease is approximately 8 percent, and 30 percent will develop degenerative macular changes consistent with earlier forms of the disease. With the expected increase in the number of older individuals in the population, AMD is predicted to increase by more than 50 percent by the year 2020, substantially increasing the societal health burden.

IDENTIFYING MARKERS

Johnson noted that a critical aspect of the new study was the reclassification of current AMD grading schemes. This particular objective of the study is to expand the AMD classification scale to better reflect the genetics associated with disease progression and to identify therapeutic targets before the disease develops into the advanced, vision-blinding form.

"By testing families with AMD-affected members, we are also likely to identify genetic variations that are unique to individual families," Johnson said. "It is also likely that several families may share a common set of genetic variations. In the likely event of identifying strong AMD genetic risk factors in these families, we will be assessing their impact in a large sample of approximately 4,500 unrelated individuals."

And if all goes as planned, future generations of seniors will have a greatly reduced chance of suffering from AMD and be able to drive wherever they wish much later in life. ▪

2012 RESEARCH

Texas Biomed Scientists Use Animal Models to Advance Medicine

RESEARCH LEADING TO ALMOST EVERY NOBEL PRIZE IN MEDICINE AWARDED SINCE 1901 HAS BEEN DEPENDENT ON DATA FROM ANIMAL MODELS OF DISEASE, A FACT THAT DRAMATICALLY DEMONSTRATES THEIR IMPORTANT ROLE IN BIOMEDICAL RESEARCH ADVANCES. SCIENTISTS AT TEXAS BIOMED AND ELSEWHERE STUDY ANIMALS TO LEARN MORE ABOUT HEALTH PROBLEMS AND TO ASSURE THE SAFETY OF NEW MEDICAL TREATMENTS.

"WE ESTABLISHED THE MONKEY MODEL FOR *research on Chagas disease* BECAUSE PROGRESS HAS BEEN EXTREMELY SLOW IN DEVELOPING CANDIDATE TREATMENTS FOR IT AND EVEN SLOWER IN DEVELOPING WAYS TO ASSESS THE EFFICACY OF *candidate treatments.*"

— JOHN L. VANDEBERG, PH.D.

Because some diseases and health problems involve processes that can only be studied in living organisms, scientists also need to understand these conditions before they can develop ways to treat them.

Recent developments during 2012 with animal models at Texas Biomed illustrate the progress and promise of biomedical research for disorders as diverse as nonalcoholic fatty liver disease, Chagas disease and liver cancer.

LIVER DISEASE

Scientists at Texas Biomed published a report showing that the laboratory opossum can serve as a new animal model to study the most common liver disease in the nation. The new study, published in the *American Journal of Physiology-Gastrointestinal and Liver Physiology*, was supported by the National Institutes of Health and the Robert J. Kleberg Jr. and Helen C. Kleberg Foundation.

The condition — nonalcoholic steatohepatitis (NASH) — resembles alcoholic liver disease, but occurs in people who drink little or no alcohol. NASH afflicts up to 15 million Americans, and there is no cure.

The major feature of NASH is accumulation of fat in the liver, along with inflammation and functional damage. Most people with NASH feel well and are not aware that they have a liver problem. Nevertheless, NASH can progress to cirrhosis, in which the liver is permanently damaged and no longer able to function properly.

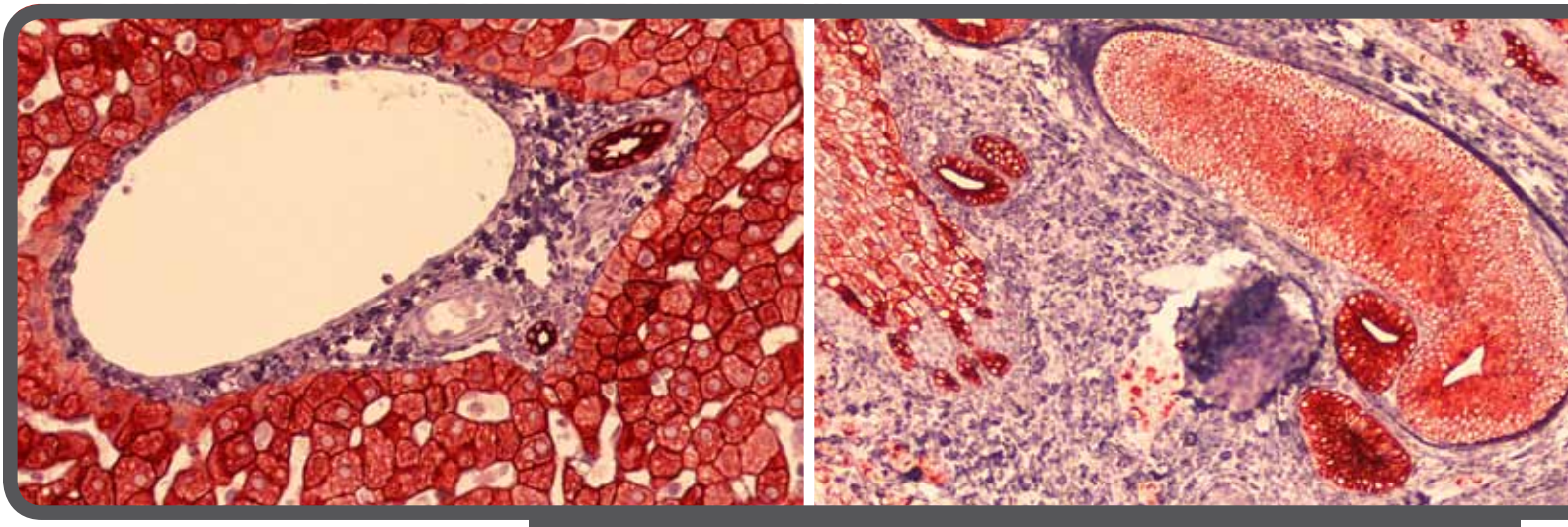
NASH-related cirrhosis is the fourth most common indication for liver transplantation in the U.S. NASH affects 2 to 5 percent of Americans. An additional 15 to 30 percent of Americans have excess fat in their livers, but no inflammation or liver damage. This condition is called "fatty liver" or nonalcoholic fatty liver disease (NAFLD), which can progress to NASH.

"This is the type of model in which to develop mechanism-based therapies," wrote Geoffrey C. Farrell, M.D., of the Australian National University Medical School in Canberra, in a journal editorial.

Both NASH and NAFLD are becoming more common, possibly because of the greater number of Americans with obesity and its important health complications: type 2 diabetes, high blood cholesterol levels, high blood pressure and other risk factors for heart attack and stroke.

In the past 10 years, the prevalence of obesity has doubled in adults and tripled in children. It was previously reported by other scientists that the prevalence of NAFLD and NASH in a group of middle-aged patients in San Antonio is 46 percent and 12 percent, respectively.

"It now seems likely that genetic factors, such as those important for diabetes and high cholesterol levels, are what determine why a small proportion of those with fatty liver develop NASH and its complications of cirrhosis and liver cancer," said Farrell.



BABOON LIVER CANCER STAINED FOR BIOMARKER CYTOKERATIN 8:

Image, left, is of a normal baboon liver showing a field of liver cells and in the middle a vein surrounded by endothelial cells.

On the right, the image shows baboon liver cancer with areas of tumor cells at the bottom left corner. Cells in the middle are not cancer, but have grown into large structures in response to the cancer.

MUTATED GENE

In the new study, high-responding opossums developed elevated cholesterol and fatty liver disease when fed a high-cholesterol and high-fat diet, whereas low-responding opossums did not. High responders carry a mutated ABCB4 gene, which affects their ability to secrete excess cholesterol from the liver into bile which, in turn, transports the cholesterol to the intestines for excretion from the body. As a consequence, opossums with the mutated gene accumulate cholesterol in the liver and ultimately in the blood.

"We showed that the fatty livers of high responders contain a tremendous amount of cholesterol," said first author Jeannie Chan, Ph.D., of Texas Biomed. "The opossum is a new animal model for investigating the mechanism by which cholesterol mediates liver injury, and that will lead to a better understanding of the role of dietary cholesterol in the development of NASH."

Co-authors on the study included Rampratap S. Kushwaha, Ph.D., Jane F. VandeBerg, and John L. VandeBerg, Ph.D., all of Texas Biomed; and Francis E. Sharkey, M.D., of the UT Health Science Center San Antonio.

LIVER CANCER

In another project, Texas Biomed's Robert Lanford, Ph.D., in 2012 reported promising results in the development of the baboon model for liver cancer that will be useful for testing new drugs and other therapeutic modalities, as well as advancements in imaging methods for early detection. The project was initiated by a pilot grant from the Voelcker Foundation and subsequent funds from the USAA and Hearst foundations and the Joe & Jessie Crump Fund of Fort Worth.

Worldwide, approximately 170 million people are chronically infected with hepatitis C virus (HCV), which frequently progresses to serious liver disease, including cirrhosis and liver cancer. Approximately 4 percent of the adult population in the United States is chronically infected with HCV, and the percentage of disease is even higher within the veteran population and the Mexican-American community in San Antonio and South Texas.

In the United States, HCV infection is the leading cause of liver transplantation, and liver cancer due to HCV infection is the most rapidly increasing cause of cancer death. Worldwide, liver cancer is the fourth leading cause of cancer death. Because it is a fast-growing tumor that is rarely diagnosed in the early stages, liver cancer is typically fatal within a year of diagnosis.

In this research, Lanford and his team first cloned baboon genes involved in liver cancer and introduced genetic modifications to convert the genes into cancer-inducing genes, or oncogenes. Using gene therapy vectors, multiple modified genes were then introduced into liver cells (hepatocytes) growing in a well-established culture system. Cells with the ability to form tumors were first introduced into a mouse model, which had no immune system and could not reject foreign tissue, to test for tumor formation. Modified hepatocytes that were capable of making tumors in mice were then introduced into the liver of the baboon that was the original donor of the cells. Using the original donor as the recipient avoided immune-mediated rejection of the tumor.

In mice, the best combination of oncogenes produced tumors in all animals within three to four weeks. In baboons, tumors were produced in 50 percent to 70 percent of animals within two to three months.

"After two years of effort, we were really excited when we detected the first tumor in a baboon using MRI imaging at the UT Health Science Center San Antonio Imaging Research Center," Lanford said.

"Once perfected, this system could be used by a drug company to tailor drugs for specific types of liver cancers in humans, especially those that rapidly become resistant to current chemotherapies," he said.

CHAGAS DISEASE

In 2012, Texas Biomed received $2 million to identify new ways of determining treatment efficacy using the cynomolgus monkey model in Chagas disease, a potentially fatal tropical

condition that affects nearly 8 million people throughout the world and hundreds of thousands in the United States.

The organization Drugs for Neglected Diseases initiative (DNDi) received an award of $3 million from the Wellcome Trust, about $2 million of which will go to Texas Biomed as a sub-contractor. VandeBerg, Texas Biomed's chief scientific officer, is the organization's principal investigator on the project. The announcement was made at the 61st annual meeting of the American Society of Tropical Medicine and Hygiene in Atlanta.

Chagas disease is the leading parasitic killer in the Americas, causing more deaths than malaria. The federal Centers for Disease Control and Prevention estimates that 300,000 or more people in the United States are infected. Moreover, health officials say that in South Texas they have identified increased numbers of "kissing bugs" that carry the parasite that causes the disease.

No easy-to-use and reliable test available can now assess if Chagas patients are rid of the parasite after treatment. Current treatment options have significant limitations due to safety considerations, inconsistent efficacy, and long treatment duration. Determining if treatment has cured the infection requires difficult, repetitive laboratory testing that, in some cases, cannot confirm if a person is cured of the infection.

Many patients and physicians are skeptical of the benefit of treatment for the chronic, indeterminate form of Chagas without a direct way to measure cure. A new, robust test for the infection would help to expand treatment, as well as provide a valuable tool for accelerating the evaluation of new drugs in clinical trials.

The $3 million Wellcome Trust award will fund the first-ever large-scale study involving treatment of nonhuman primates naturally infected in their outdoor living environment with *Trypanosoma cruzi*, the parasite that causes Chagas disease. Cynomolgus monkeys will be treated with three drug regimens versus placebo: benznidazole at optimal dose, benznidazole at suboptimal dose and another azole compound with antiparasite activity.

Over a period of 12 months after treatment, the animals will be examined for clearance of the Chagas parasite through polymerase chain reaction and other tests. The primary goal of the study is to see if any of these tests can accurately measure parasitological cure.

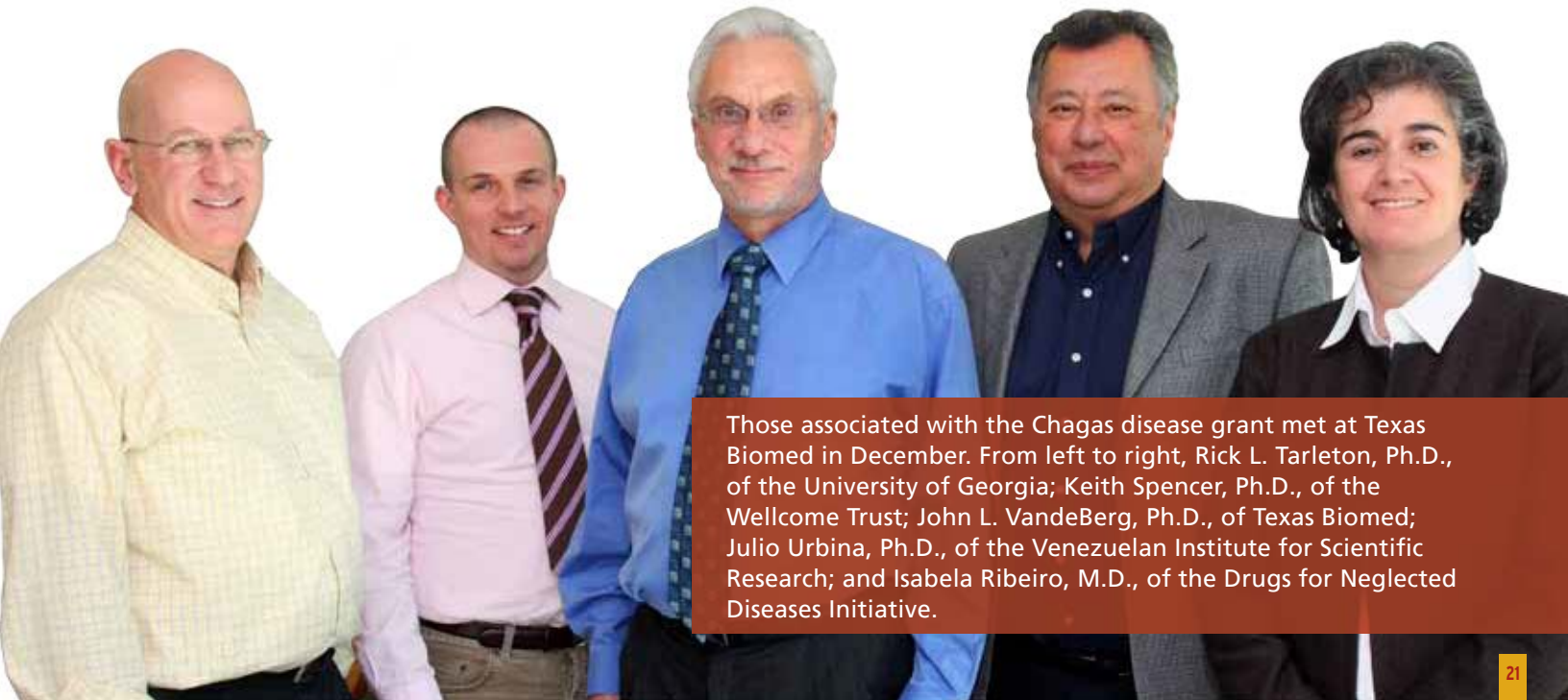
"We established the monkey model for research on Chagas disease because progress has been extremely slow in developing candidate treatments for it and even slower in developing ways to assess the efficacy of candidate treatments," said VandeBerg. "The research supported by this grant will greatly enhance our capacity to assess the efficacy of existing candidate treatments for Chagas disease, as well as treatments that will be developed in the future."

"We need to be able to tell patients whether or not their treatment has worked," said Graeme Bilbe, Ph.D., research and development director for DNDi. "The results of this study could encourage treating more patients now with what we have and facilitate future clinical trials of new treatments for chronic Chagas disease patients."

The project was initiated by VandeBerg and Rick Tarleton, Ph.D., of the Center for Tropical and Emerging Global Diseases at the University of Georgia. The study will be coordinated by DNDi and run until 2015. Texas Biomed will conduct the experimental protocols with the animals and, along with the University of Georgia, conduct biomarker analysis.

Other partners conducting testing will be the University of Texas at El Paso and the Argentinean National Council of Scientific and Technical Investigation. To facilitate future biomarker discovery efforts, the biological samples collected in the study will be stored at Texas Biomed and made available to other researchers.

And if all goes as planned, new preventions and treatments for nonalcoholic fatty liver disease, liver disease and Chagas disease may soon become available as animal models pave the way for scientific and medical advances. ▪



Those associated with the Chagas disease grant met at Texas Biomed in December. From left to right, Rick L. Tarleton, Ph.D., of the University of Georgia; Keith Spencer, Ph.D., of the Wellcome Trust; John L. VandeBerg, Ph.D., of Texas Biomed; Julio Urbina, Ph.D., of the Venezuelan Institute for Scientific Research; and Isabela Ribeiro, M.D., of the Drugs for Neglected Diseases Initiative.

2012 RESEARCH

New Methods Advance Ways to Outsmart Toxic Agents, Deadly Viruses

WITH THE WORLD GEOPOLITICAL SITUATION CONTINUING TO BE UNSTABLE AND UNPREDICTABLE, TEXAS BIOMEDICAL RESEARCH INSTITUTE VIROLOGISTS REPORT NEW FINDINGS ON FASTER, LESS EXPENSIVE ROUTES TO SCREEN TOXIC AGENTS AND DEVELOP COUNTERMEASURES, AND THE REPURPOSING OF EXISTING CANCER DRUGS TO BLOCK A POTENTIAL THREAT.

"BEING ABLE *to respond quickly to known biological threats* WILL BETTER PREPARE US FOR COMBATING EMERGING AND ENGINEERED THREATS OF THE FUTURE."

— ANDREW HAYHURST, PH.D.

Both developments represent advances in Texas Biomed's continuing efforts to prevent and treat diseases that could be caused by biological warfare.

The new screening process looks for pairs of affinity reagents – molecular magnets that bind to and hold on to their targets, such as toxins, viruses or bacteria. The system will enable biothreat assays to be identified and assembled much faster than methods now in use.

"Using crude extracts from engineered *E. coli*, the workhorse bacterium of the biotechnology laboratory, the new route bypasses the need for purification and complex equipment, making it possible for screening to be performed in under an hour," said Texas Biomed researcher Andrew Hayhurst, Ph.D.

The basis for how the system works is engineering the bacteria to add a single molecule of biotin (vitamin B7) to the molecular magnets they produce and then splitting them to create "captors" and "tracers" that can be completely discriminated from each other. Normally, extensive and time-consuming modifications of one half of the population would be required to make tracers distinct from captors. By using an old yet highly efficient method available to all, this is performed within the minute by a molecular game of hide and seek.

"He's working on a detection system that can be readily used in developing countries," said Jean L. Patterson, Ph.D., the Virology and Immunology Department chair. "If all goes well, it will be as sensitive as a laboratory based system but at the same time hardy enough to survive sub-Saharan temperatures."

The process – funded primarily by Texas Biomed and the San Antonio Area Foundation and in part by the Defense Threat Reduction Agency and the National Institutes of Health (NIH) – was described in Nature Publishing's *Scientific Reports*.

A SIMPLE SCREEN

Hayhurst's surprisingly simple scheme allows scientists to make stop-gap tests to any given biological threat in a matter of days, with the screening step completed in an hour. The goal now is to speed up the entire process to work within a single day. He initially developed the pipeline using llama antibodies as the affinity reagents to botulinum neurotoxins, known as the world's most poisonous poisons – 100 billion times more toxic than cyanide and handled in a specialized biosafety cabinet at biosafety level 2.

Satisfied that the system was working, he then took it into Texas Biomed's biosafety level 4 laboratory with his assistant, Laura Jo Sherwood, and they generated a stop-gap test for Ebola virus Zaire in days. This virus has been shown to be 95 percent lethal in outbreak settings and there is no vaccine or therapeutic treatment for it. It can be a risk to the United States through importation and misuse.

RESPONDING TO THREATS

Botulinum neurotoxins and Ebola virus are among a handful of threats now categorized as Tier 1 agents, presenting the greatest risk of deliberate misuse with the most significant potential for mass casualties or devastating

effects to the economy, critical infrastructure and public confidence.

"Being able to respond quickly to known biological threats will better prepare us for combating emerging and engineered threats of the future," Hayhurst said. "However, the great thing about this test pipeline is that it can be applied to almost any target of interest, including markers of diseases like cancer."

This last point is very important as the vast majority of researchers do not work on biothreats, but do have favorite targets of interest for which they can assemble proof of concept assays with minimal equipment. The massive global effort to unravel the secrets of the proteomes of various organisms including humans demands assays for thousands of unique targets and this pairing system is well suited to that role.

Texas Biomed has applied for a patent on the process, which could be licensed to companies for developing diagnostics to specific medical conditions, tests for environmental monitoring or to accelerate in-house research programs. Importantly, academic and non-profit researchers will always be able to use the process freely.

DISABLING EBOLA

In other work at Texas Biomed, two currently used leukemia drugs blocked the deadly Ebola virus from reproducing in the test tube — an early, promising advance in a disease and potential biological weapon with no approved treatments or vaccine.

Testing of the drugs took place in the biosafety level-4 lab at Texas Biomed, under the direction of co-author Ricardo Carrion Jr., Ph.D., in collaboration with government scientists and researchers in Houston and Atlanta.

The two drugs, nilotinib and imatinib, don't attack the virus directly, but instead target the patient's own infected cells, preventing the virus inside from reproducing and escaping.

"That's a concept that's been attractive for antiviral therapy, because if you can target a cellular protein that's required for the virus, it makes it a little harder for the virus to mutate to develop resistance," said Gary Nabel, M.D., Ph.D., former director of the Vaccine Research Center at the National Institute of Allergy and Infectious Diseases, who led the study published in *Science Translational Medicine*.

And while the drugs didn't completely clear the virus, researchers say what they've learned from outbreaks of the disease in Africa shows that those with low levels of the virus in their bodies often survive.

The hope would be that a short-term course of treatment with the drug might eliminate enough of the virus that the patient's own immune system could eliminate the rest. The goal of this research is to shave some of the viral load off of the infection, lowering it tenfold, to give people a chance to survive. Nabel cautioned that the work is early but promising, and that the next step is to test it in animals. Because Ebola outbreaks in nature are so infrequent and unpredictable, it makes human testing almost impossible, researchers say.

"Ebola virus shares some of the same cellular pathways as leukemia," noted Patterson. "And since the leukemia drugs are already approved, this means that they may quickly become useful for Ebola if animal tests prove successful."

Government rules will allow approval of vaccines and treatments in such cases if they demonstrate effectiveness in two animal models.

Ebola hemorrhagic fever, described by the World Health Organization as often fatal and one of the most virulent viral diseases on the planet, was named for a river in the Democratic Republic of the Congo, near the location where it was first identified in 1976. It causes illness in both people and nonhuman primates, and appears sporadically in a handful of African nations.

"Outbreaks of Ebola virus are unpredictable," said Carrion. "We're still trying to identify the reservoir. We don't even know what maintains it in nature."

But the pieces of the puzzle may now be coming together. ■

QUICKER, CHEAPER ROUTE TO TESTS FOR DISEASES

Texas Biomed scientists have invented faster and more economical ways to assemble biodetection tests capable of identifying any given target of interest such as toxins, bacteria, viruses or human protein markers of disease.

CURRENT PROCESSES	TEXAS BIOMED'S PROCESS
TIME	
Current methods to assemble tests can take several days for each small batch of components and may require further modifications over weeks.	Texas Biomed's process can be applied to hundreds of components in a matter of hours to guide scientists to a suitable starting test for further development.
EQUIPMENT AND ENVIRONMENT	
Current methods can demand complex, sensitive and very costly instruments thereby increasing maintenance burdens and stasis in a controlled environment.	Texas Biomed's process works without the need for complex equipment thereby reducing costs and enabling mobility.
LABOR AND ACCURACY	
Current methods require a lot of hands-on time at several sophisticated steps, and can be prone to human error, which pushes up costs and increases development time.	Texas Biomed's process is straightforward and reliable, thereby reducing human error and also making test development a reachable goal for all labs.

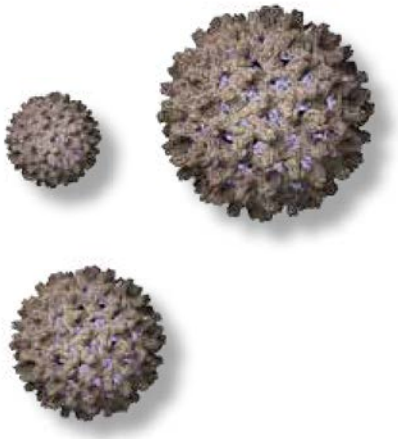
2012 RESEARCH

Optimism in Fighting Hepatitis C, the "Silent Epidemic"

ALTHOUGH INFECTION WITH THE HEPATITIS C VIRUS (HCV) REMAINS AN EPIDEMIC ACROSS THE GLOBE AND IN THE UNITED STATES, INTENSE EFFORTS BY RESEARCHERS AT TEXAS BIOMED AND ELSEWHERE ARE CREATING OPTIMISM THAT NEW AND BETTER TREATMENTS ARE ON THE HORIZON.

"IT IS CLEAR THAT PATIENTS WILL SOON HAVE A NUMBER OF *options for true cures* FROM THE VIRUS THEY HAVE CARRIED FOR DECADES."

— ROBERT LANFORD, PH.D.



Several combinations or "cocktails" of antiviral drugs are in the final stages of human clinical trials. These cocktails cured up to 95 percent of patients in the trials in only 12 weeks and without the harsh side effects of interferon, which is now part of the standard treatment.

"It is clear that patients will soon have a number of options for true cures from the virus they have carried for decades," said Robert Lanford, Ph.D., a virologist who has been working at Texas Biomed on hepatitis C treatments and vaccines for 25 years.

The federal Centers for Disease Control and Prevention (CDC) estimates that 170 million people are infected with HCV globally, including more than 3 million people in the United States. HCV contributes to the deaths of 15,000 Americans annually and the numbers are rapidly rising. Three out of four Americans with hepatitis C are unaware of their infection and thus cannot seek treatment or alter their lifestyle to slow the progression of disease. Two-thirds of the infected population are baby boomers, prompting the CDC to urge primary physicians to screen everyone aged 45 to 64.

Since hepatitis C infection is typically mild in its early stages, it is rarely diagnosed and is often not recognized until it progresses to severe liver disease. With a typical cycle of disease from infection to advanced liver disease taking 20 to 30 years, the true impact of this disease on a growing infected population will not be apparent for many years, hence the term "silent epidemic."

NEW DRUGS

Within the last two years, the U.S. Food and Drug Administration (FDA) approved two new drugs for the treatment of HCV genotype 1, the most common type in the United States. The drugs, called protease inhibitors, are the first new drugs approved for HCV infection in a decade.

The good news is that these drugs cure up to 75 percent of patients, leaving them free of the virus. The bad news is that the new drugs must still be used in combination with conventional therapy. The standard treatment for hepatitis C has been a combination of two drugs, pegylated-interferon and ribavirin, which are taken for a year. For many patients, the side effects of this therapy are too severe to tolerate.

In collaboration with major pharmaceutical companies, Texas Biomed's Southwest National Primate Research Center demonstrated the safety and efficacy of many of these antivirals using the chimpanzee, the only animal other than man that is susceptible to HCV infection.

In addition to the therapies for elimination of the virus from infected patients, advances are being made to improve the outcome of liver transplantation. For some patients, the new antiviral cocktails will be too late. HCV-induced cirrhosis and liver cancer are the leading indication for liver transplantation, accounting for about half of the 6,000 liver transplants each year in the United States.

For patients with end-stage liver disease from HCV infection, liver transplantation is the only option. While it can be a life-saving treatment, transplantation does not cure the disease. In nearly all cases, the patient's new liver is eventually infected by HCV because the virus

remains in the patient's bloodstream during surgery. The course of recurrent HCV disease is accelerated after transplantation, and up to 20 percent of transplant patients develop cirrhosis within five years.

In recent promising advances, a monoclonal antibody, developed by MassBiologics of the University of Massachusetts Medical School and tested in the chimpanzee animal model at Texas Biomed, was found to block infection of the liver by HCV. In the study, researchers found that the human monoclonal antibody targeting the virus protected chimpanzees from HCV infection in a dose-dependent manner.

The new report by scientists from MassBiologics, Texas Biomed, the National Institutes of Health (NIH), and Merck Research Laboratories, funded by MassBiologics and NIH, appeared in the journal *PLOS Pathogens*. Researchers had previously demonstrated that the monoclonal antibody, called HCV1, blocks HCV from infecting liver cells in laboratory tissue culture.

PROOF OF CONCEPT

"This is an important preclinical proof-of-concept study demonstrating that a high dose of neutralizing antibody can protect the liver from HCV infection using monoclonal antibodies," said Lanford, a study co-author.

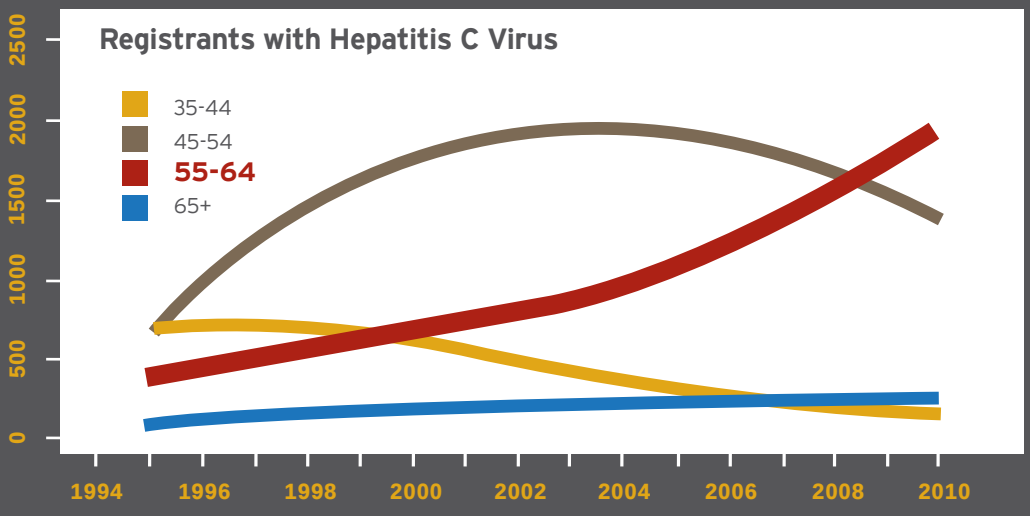
"One can envision improving on these results with a cocktail of antibodies or by using this antibody with some of the newer antivirals currently in clinical trials. Infection of the new donor liver by residual virus in the patient is one of the major obstacles preventing a full recovery in these patients," he added.

With new avenues for treatment such as the antiviral cocktails and monoclonal antibodies, the odds for successfully treating infected patients and liver transplant candidates are rapidly improving and should continue to rise markedly in the near future. ▪

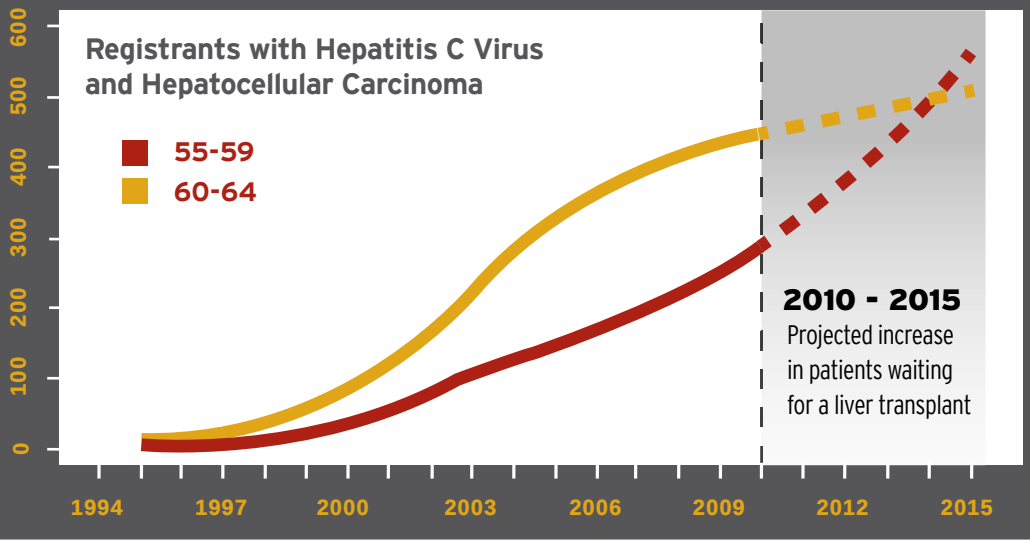
INCREASE IN HEPATITIS C DIAGNOSIS, WAITING LIST INCREASE FOR LIVER TRANSPLANT

Hepatitis C virus (HCV) is a silent epidemic that is often not recognized until progression to severe liver disease.

Diagnosed with Hepatitis C Virus: Since hepatitis C infection is rarely diagnosed early, it is often not recognized until progression to severe liver disease in people ages 55 - 64. The chart on the right reflects this age group's progression of diagnosis over the last 16 years.



Waiting for Liver Transplant: The number of patients waiting for liver transplants has also increased since 1995, and is projected to continue for patients in both the 55 - 59 and 60 - 64 age groups.



TEXAS BIOMED PROFILE

Marsha Sojot Plays Gatekeeper for Virology and Immunology Department

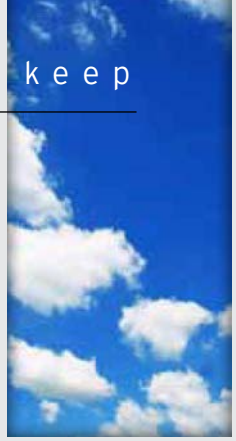
AFTER 20 YEARS IN THE AIR FORCE, MARSHA SOJOT TRADED 12-HOUR DAYS OF REAL LIFE INTRIGUE FOR FIGHTING THE EVIL MONSTERS OF THE FANTASY ONLINE WAR GAME WORLD OF WARCRAFT. AT MORE THAN FIVE HOURS EVERY DAY, THE TIME SHE DEVOTES TO THE GAME CAN, AT TIMES, DRIVE HER FAMILY NUTS.

But it's this same passion that Sojot, with her many years of experience, brings to her job as the Virology and Immunology Department's administrative and project support specialist and facility security officer. She's the top assistant to Department Chair Jean L. Patterson, Ph.D.

As a member of her parents' and then her own military family, Sojot has been so many places, it's difficult to know where to start. She was born in San Diego to Navy parents. Her early high school years were spent in Honolulu, and then she finished up in Huntington, West Virginia.

"My girlfriends and I hung out with college guys during my senior year. The high school there reminded me so much of the movie Grease," she recalled.

Her own Air Force career sent her to many states, including California, Hawaii, Arizona, Virginia, and twice to Texas. Throughout, Sojot has paid minute attention to detail, whether working her first job as a 17-year-old apartment manager, or serving two years at the Pentagon on the personal staff of Gen. John Shalishkavili, the chairman of the Joint Chiefs of Staff, and his successor Gen. Henry Shelton.



"A LOT OF ROUTINE THINGS FILL UP THE DAY; BUT EVERY NOW AND THEN SOMETHING UNIQUE POPS UP, AND THAT IS ALWAYS EXCITING. ONE DAY, THAT ONE EXCITING AND UNIQUE THING THAT POPS MAY JUST BE *a cure for a deadly virus. You just never know.*"

– MARSHA SOJOT

She joined the Air Force on a dare from her husband, Charles, also an Air Force veteran. After her 20 years in the Air Force ended with a stint at Lackland AFB working with the Army and Air Force Exchange Serve, Charles saw a job listing in the newspaper for Texas Biomed and told her she "should get a real job." Later, Charles quit his job as a guard at the Federal Reserve in San Antonio to work as the laboratory glassware specialist in the same department at Texas Biomed.

Marsha Sojot's military career highlight was the two years she served as part of the personal staff to Gens. Shalishkavili and Shelton. For a retirement gift, her office arranged for a private evening tour of the White House where she and Charles visited the Oval Office and the War Room, saw a charred beam remaining from when the building was torched during the War of 1812, and admired Gilbert Stuart's portrait of George Washington.

So what does Sojot do at Texas Biomed?

"Basically, whatever comes up and then some. I'm always here to assist — working directly with Dr. Patterson, labeling tubes for the lab folks, escorting vendors for equipment repairs, making arrangements for trips of researchers around the world, preparing correspondence, writing purchase requisitions, processing time sheets," she said. "A lot of routine things fill up the day; but every now and then something unique pops up, and that is always exciting. One day, that one exciting and unique thing that pops may just be a cure for a deadly virus. You just never know."

She noted a big difference between her former colleagues in the military, many of whom she had to train and supervise, and her co-workers at Texas Biomed, who are self-sufficient and highly educated. Most people join the military to get an education while people at Texas Biomed have already accomplished those goals.

"My first impression of Marsha was that she seemed like a very nice person with a great sense of humor," said Patterson. "I hired her because we needed someone who had worked with sensitive subjects and could maintain confidential material. She was a veteran who had risen to the rank of master sergeant working for the Pentagon and the Joint Chiefs. She has great administrative and computer skills, works with all of the principal investigators on their needs, manages all of the accounts of the department, handles sensitive material and communicates effectively with others outside the department."

"Her primary personal characteristic is the ability to get along by treating everyone fairly and kindly," Patterson said.

"She's the cream of the crop, very professional, and the virology department security chief," said Kim Vogel, who is responsible for environmental health and safety and has worked closely with Sojot entering select agent inventory for the biosafety level 4 laboratory (BSL-4).

Sandra Rios, who coordinates department meetings and other issues related to the BSL-4 with Sojot, said: "She's always professional, detailed, punctual, and regimented in the best sense of the word."

As the department's "gatekeeper," Sojot takes care of all the badges giving access to the various labs and keys and entry codes when needed. She responds to any alarm that goes off, regardless of the time of day or night. She prepares scientific summaries and the departmental budget and gathers all the personnel reviews for submission. Basically, she's the first person people see in their contact with the department, and she keeps everything running smoothly.

Sojot has been at Texas Biomed for 12 years, her longest tenure in any one job, and has no plans to go anywhere else. At the moment, she's extra busy outside of work, caring for the home she and Charles built in 1991 in northwest San Antonio. She's enthralled by the release of a new World of Warcraft edition called "Mists of Pandaria." She took two days of vacation just to play. Her kids shake their heads and roll their eyes when they see her reading gaming magazines.

She and Charles have two grown sons, Lee and Christopher, and a granddaughter, Tianna.

Her other hobbies include reading, watching movies, photography, gardening, and taking care of six dogs (Joey, Toby, Phoebe, Milly, Rachel, and Rocky), five cats (Spice, Alvee, Sima, Theo, and Cindy) and a guinea pig, Lucy.

Any favorite destinations?

"Everyone who knows me knows I usually travel to only two places for fun: Florida and Las Vegas."

Ever the gamer. ■

General John Shalishkavili, Chairman of the Joint Chiefs of Staff, with Marsha Sojot, saying farewell to his personal staff upon his retirement in 1997.

YEAR IN REVIEW

San Antonio City Manager Sheryl Sculley discusses the importance of collaboration at a City Hall news conference announcing the establishment of the San Antonio Vaccine Development Center. Texas Biomed President and CEO Kenneth P. Trevett played a critical role in organizing the center, which involves scientists from the UT Health Science Center San Antonio, the Southwest Research Institute, the University of Texas at San Antonio and Texas Biomed.

MANY EVENTS DURING 2012 MARKED THE TEXAS BIOMEDICAL RESEARCH INSTITUTE'S CONTINUING SUCCESS IN PRODUCING FIRST-RATE SCIENCE, EXPANDING ITS SCIENTIFIC RESEARCH CAPACITY, AND RAISING ITS PROFILE IN SAN ANTONIO, THE NATION AND BEYOND. HIGHLIGHTS INCLUDED RECOGNITION OF THE WORK OF INDIVIDUAL SCIENTISTS AND NEW COLLABORATIONS WITH OTHER SAN ANTONIO RESEARCH INSTITUTIONS.

GROUNDBREAKING MALARIA RESEARCH

The malaria work in Southeast Asia of Texas Biomed geneticist Tim Anderson, Ph.D., and his collaborators was widely publicized in the international news media. The scientists documented the emergence of resistance to the anti-malaria drug artemisinin in western Thailand, creating a critical point in global efforts to control the disease. They also found a major region of the malaria parasite genome associated with resistance, raising the hope that there will soon be effective molecular markers for monitoring the spread of resistance.

The achievements of Anderson's laboratory during 10 years of work on the evolution and spread of resistance to antimalarial drugs were recognized by a MERIT award from the National Institutes of Health. This award extends the laboratory's current five-year, $3 million grant for this work by three to five more years (until 2019-2021) without the need for additional review. The MERIT award program exists to extend funding for experienced researchers who have made a significant and sustained impact in a high-priority research area and is a symbol of scientific leadership in the research community.

OUTREACH TO SAN ANTONIO AND BEYOND

During 2012, 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 and Technology Foundation and on the advisory boards of the Southwest Research Institute and of St. Jude Children's Research Hospital. He is also a member of the executive committee of United Way.

Trevett was reelected chair of BioMed SA, a nonprofit organization that 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 highlighting the city's leadership in health care and bioscience.

Texas Biomed is an active member of the Association of Independent Research Institutes (AIRI) and played a significant role at its 2012 annual meeting. Gregory M.L. Patterson, Ph.D., Texas Biomed's vice president for research operations, serves as AIRI president-elect and will become president in 2013. He was secretary of its board of directors and a 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, serves as a member of the SCAW board of trustees.

Texas Biomed representatives in 2012 visited the offices of the San Antonio Congressional delegation and other national legislators to educate them about the continuing need for the use of nonhuman primates, including chimpanzees, baboons, and monkeys, in biomedical research. On this issue, Texas Biomed was featured in two major news broadcasts: NBC's *Rock Center with Brian Williams* and the Public Broadcasting System's *NewsHour*.

During the first three months of 2012, Texas Biomed opened its doors to seven classes of high school seniors when the Texas Biomedical 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 (SNPRC) and speaking with Texas Biomed scientists working on hepatitis C, heart disease, diabetes, obesity, and other health problems.

In June, Texas Biomed was visited by 18 San Antonio area high school science teachers. Jerilyn Pecotte, Ph.D., and Corbett Christie, vice president for institutional advancement, organized the day's events. Activities included a welcome from Kenneth P. Trevett, a briefing and tours of the primate center animal colonies, AT&T Genomics Computing Center and laboratories.

In October, Texas Biomed hosted a meeting of the eight national primate research centers and organized the annual Nonhuman Primate Models of AIDS Symposium, which was held in San Antonio.

Texas Biomed signed a memorandum of understanding with the Mexican Health Foundation, a nonprofit civil association focusing on scientific and technological knowledge and the study of health policies. The two organizations agreed that it was their "intention to pursue and develop research projects in Mexico and to improve the quality of genetic research on metabolic diseases in that country by improving scientific infrastructure and transferring technological skills in order to generate and achieve knowledge in research and in genomic medicine." Mercedes Juan, M.D., one of the signers of the document, later was appointed Mexico's secretary of health by newly inaugurated President Enrique Peña Nieto.

NEW VACCINE CENTER

President and CEO Trevett played a critical role in the establishment of the new San Antonio Vaccine Development Center, involving scientists from the UT Health Science Center San Antonio, the University of Texas at San Antonio and the Southwest Research Institute, as well as Texas Biomed. The partnership, announced at a City

Malaria Research Team: Shalini Nair, Ian Cheeseman, Ph.D., Tim Anderson, Ph.D., and Standwell Nkhoma, Ph.D.

Mexican health experts and Texas Biomed officials met to sign a memorandum of understanding for future genetic studies. Seated, left to right, are Esther Gallegos, Ph.D., of the University of Nuevo Leon School of Nursing; Mercedes Juan, M.D., Mexico's Secretary of Health and formerly President of the Health Foundation of Mexico; Kenneth P. Trevett, President and CEO of Texas Biomed; and Sarah Williams-Blangero, Ph.D., chair of the Department of Genetics at Texas Biomed. Standing, left to right, are: Saroja Voruganti, Ph.D., and Raul Bastarrachea, M.D., of Texas Biomed; Jose Maria Remes, M.D., of the University of Veracruz; Guillermo Melendez, M.D., of the Health Foundation of Mexico; and Harald Goring, Ph.D., and Shelley Cole, Ph.D., of Texas Biomed.

Hall news conference in April, has already raised $600,000 and has applied for $300,000 more in state funding.

The first annual vaccines symposium sponsored by the Center was held in the fall and included presentations by scientists from the four institutions.

The keynote speaker was Roy Curtiss II, Ph.D., of Arizona State University and a world-renowned expert on Salmonella-vectored vaccines, addressing a range of conditions from infectious diseases to cancer. The symposium included nine speakers and 39 poster presentations.

TRANSITIONS

In 2012, Thomas Folks, Ph.D., SNPRC associate director for research resources, retired after five years at Texas Biomed.

"Tom has had a major impact on the development of our center, beginning with the preparation of the base grant competing renewal application that was submitted shortly after his arrival, through his recent leadership role in organizing the nonhuman primate models of AIDS symposium," said John L. VandeBerg, Ph.D., SNPRC director and Texas Biomed's chief scientific officer.

In addition, Louis M. Gunnels, a well-regarded stockroom leader, retired after 40 years.

GREEN INITIATIVES

Texas Biomed has implemented several initiatives and programs to enhance the environmental sustainability of its facilities and operations and to promote a healthier workplace environment for its employees.

Hazardous waste generation is minimal as most laboratories are biological and not chemical, with low volumes of hazardous materials removed and environmentally processed by a certified chemical waste disposal contractor.

A comprehensive recycling program includes office paper, plastics, cardboard, scrap metal, batteries, fluorescent bulbs, computer hardware, printer ink cartridges, oils and paints. In a significant step toward becoming a more paperless facility, an Oracle system that involves human resources, payroll, purchasing, accounts receivable, accounts payable, and grants and financial accounting was installed.

Within the last two years a special study by professional energy engineers to identify areas where energy consumption at Texas Biomed could be reduced found estimated potential reductions of about 23 percent for gas and 3.5 percent for electricity. Implementation of these projects is targeted to begin during the first quarter of 2013.

In addition, design of the 70,000-square-foot Earl Slick Building, a combination laboratory and office facility, includes specifications to achieve certification from the U.S. Green Building Council's Leadership in Energy and Environmental Design rating system. ▪

Thomas Folks, Ph.D., retired after five years at Texas Biomed.

FINANCIALS

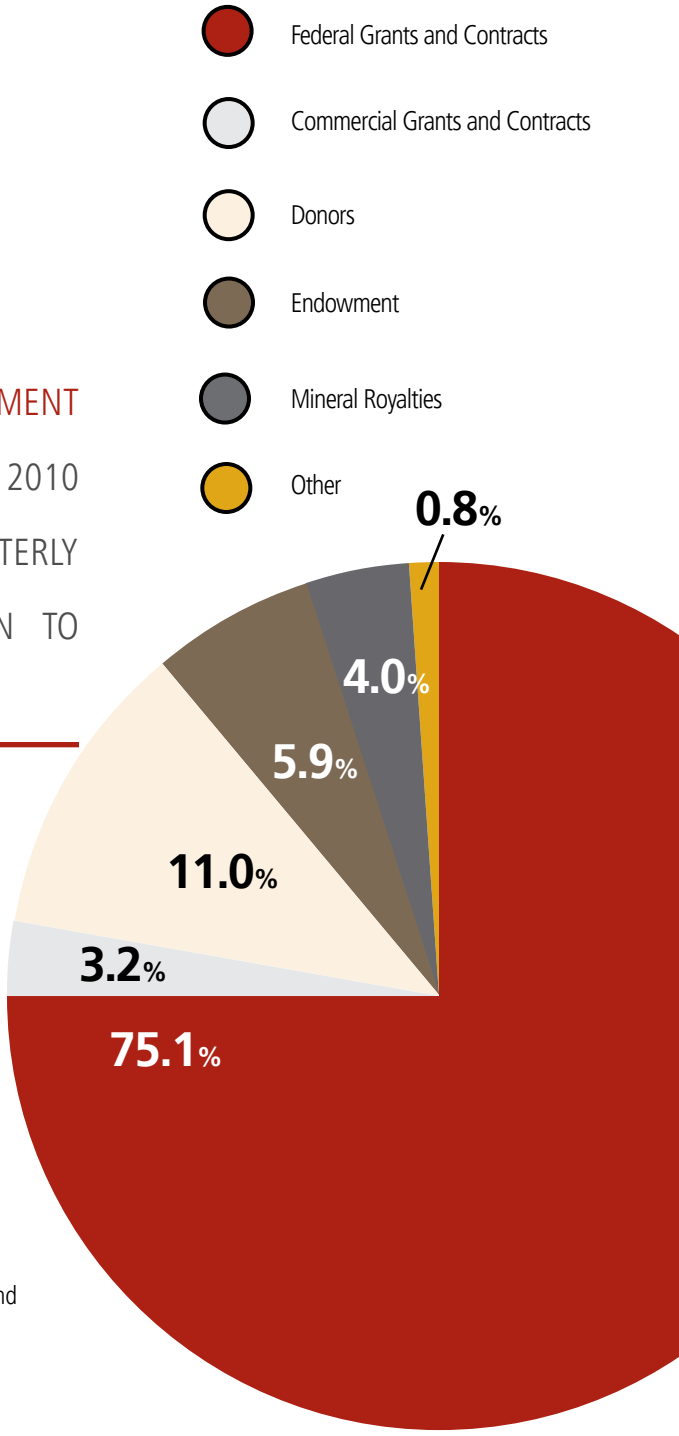
Financial Performance in 2012

THE FINANCIAL RESULTS FOR 2012 SHOWED IMPROVEMENT OVER BOTH THE ACTUAL AND BUDGETED 2011 AND 2010 TOTALS. SENIOR MANAGEMENT CONTINUED THE QUARTERLY FINANCIAL REVIEWS THAT PROVIDE TIMELY REACTION TO ONGOING FINANCIAL CHALLENGES.

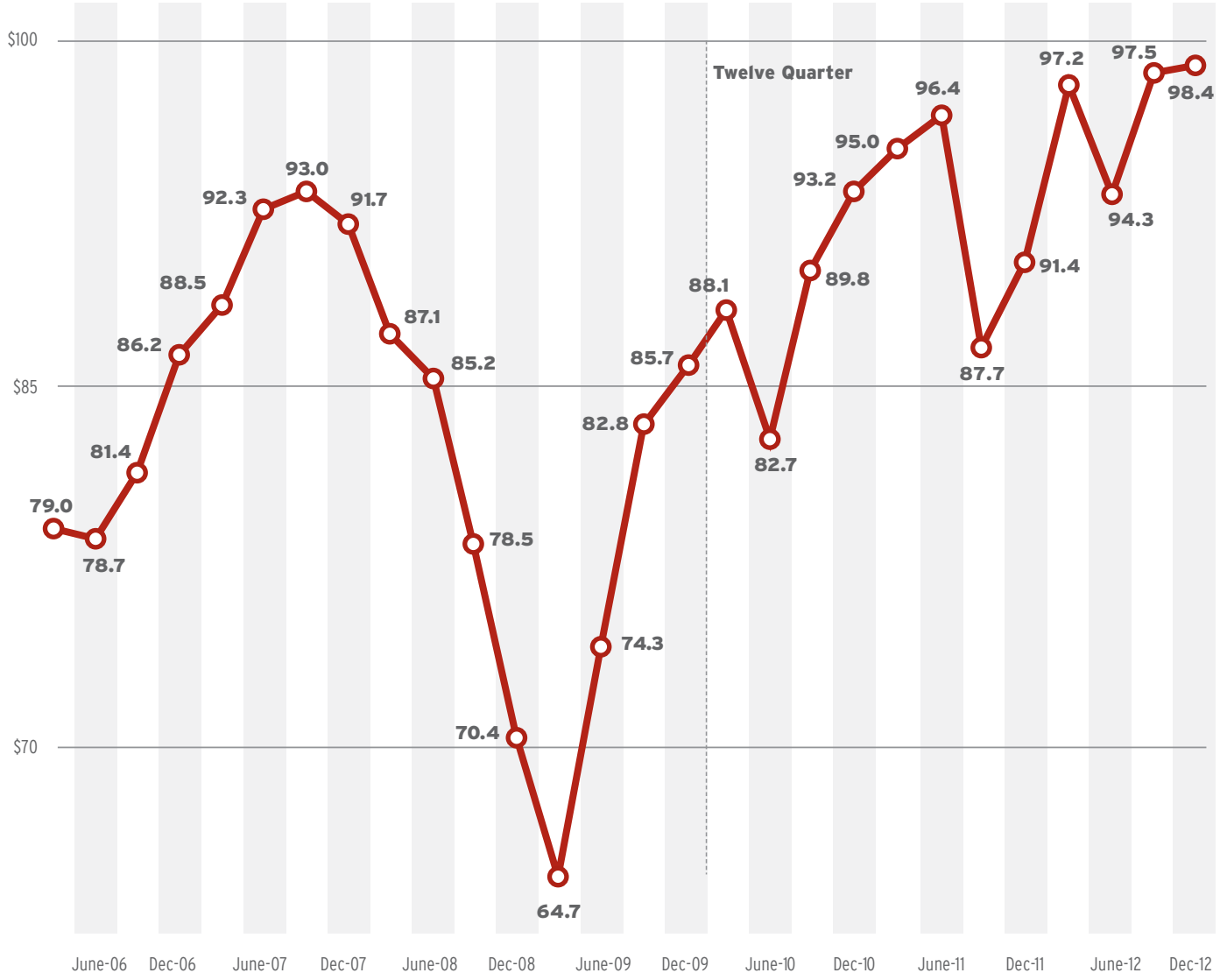
Successful negotiations on health care premiums lowered costs to Texas Biomed by nearly $500,000 in 2012, as well as providing new choices and reduced premiums for employees. As a result, Texas Biomed was able to achieve gains from operations substantially better than the budget of $306,000.

Ernst & Young's audit of Texas Biomed's operations for the fiscal year ending December 31, 2012, is expected to be completed in late spring 2013. 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 2012 will be available in the summer of 2013. Copies may be obtained through the Institute's Vice President for Finance and Administration and Chief Financial Officer Jeannie Frazier (210-258-9404).

Approximately three-quarters of Texas Biomed's funding in 2012 came through highly competitive, peer-reviewed research grants and contracts from the National Institutes of Health and other federal agencies. A growing portion of this revenue is from federal contracts for research in the BSL-4 virology laboratory. Augmenting this, approximately 3 percent of the Institute's operating revenue came from commercial contracts with biotechnology firms and pharmaceutical companies.



TEXAS BIOMED VALUE OF ENDOWMENT



Philanthropy will play an even bigger role than usual in 2013 as construction payments on the new building are made. Those amounts will appear on the financials as Assets Released from Restrictions as the donations used to construct that building are spent. These initial expenditures in 2012 pushed the portion of revenues from donors from its usual level of approximately 20 percent of income to nearly 22 percent. In 2013, this proportion will rise again as the bulk of the building construction costs are incurred.

Funds generously contributed by the Ewing Halsell Foundation in 2011 to recruit Robert Davey, Ph.D., a noted virologist, continued to support his integration into Texas Biomed. Financial support such as this from donors enables Texas Biomed to attract and retain the world's top scientists, equip state-of-the-art laboratories and provide 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 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 Texas Biomedical 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. At the end of 2012, Texas Biomed's endowment hit its all-time high, over $98.46 million. The Investment Committee of the Board of Trustees continues its efforts both to increase the endowment balance and to 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, constituting 4 percent of total revenue, provides a stable source of funding at a time when the competition for federal grant funding is increasing and federal funds for research are being limited. ▪

2012 NEW GRANTS AND CONTRACTS AWARDED

FEDERAL RESEARCH GRANTS AND CONTRACTS	PRINCIPAL INVESTIGATOR	LENGTH	TOTAL AMOUNT TO TEXAS BIOMED
National Institutes of Health (NIH) *Whole Genome Sequencing to Identify Causal Genetic Variants Influencing CVD Risk*	Dr. Joanne Curran Dr. John Blangero	5 Yrs.	**$6,092,965**
NIH *Therapy of Dengue with Modified Antibodies in Humanized Mice*	Dr. Rebeca Rico-Hesse	4 Yrs.	**$3,201,274**
Department of Defense *In Vitro and in Vivo Characterization of Filoviruses*	Dr. Jean Patterson Dr. Ricardo Carrion, Jr. Dr. Anthony Griffiths	1 Yr.	**$2,398,170**
NIH *Establishment of a SPF Rhesus Macaque Colony*	Dr. John L. VandeBerg	3 Yrs.	**$2,369,031**
NIH *Comprehensive SNP Discovery in SLC2A9, A Candidate Gene for Uric Acid Nephropathy*	Dr. Venkata Saroja Voruganti	4 Yrs.	**$1,515,524**
NIH *Characterization of a Mendelian Form of Psychosis in a Population Isolate*	Dr. Laura Almasy	2 Yrs.	**$1,334,778**
NIH/Oregon Health & Science University *A Joint Linkage/Association Strategy to Interrogate AMD Genetic Susceptibility*	Dr. Matthew Johnson	5 Yrs.	**$1,329,811**
NIH/Lovelace Respiratory Research Institute *Nonhuman Primate Model for Filovirus Vaccine Immunogenicity and Efficacy Testings*	Dr. Ricardo Carrion Jr.	2 Yrs.	**$1,274,996**
NIH/Crucell *Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (Studies 1C, 3C, 6A, and 6B)*	Dr. Jean L. Patterson	1 Yr.	**$1,199,464**
NIH *1/5 - Genetics of Transcriptional Endophenotypes for Schizophrenia*	Dr. Laura Almasy	3 Yrs.	**$1,091,383**
NIH/University of Texas Health Science Center San Antonio *Developmental Programming by Mismatch of Pre- and Postnatal Nutrition*	Dr. Robert E. Shade	5 Yrs.	**$1,024,354**
NIH/Johns Hopkins University *Arsenic Exposure, Genetic Determinants, and Diabetes Risk in a Family Study*	Dr. Shelley Cole	4 Yrs.	**$504,613**
NIH/Fisher BioServices *Efficacy of MVA-BN-Marv Vaccine Supplement*	Dr. Jean Patterson Dr. Ricardo Carrion Jr.	11 Mos.	**$503,302**
NIH/University of California Santa Cruz *Hybrid Integrated Molecular Analysis (HIMAS) for Point-of-Care Diagnostics*	Dr. Jean L. Patterson	5 Yrs.	**$468,702**
NIH *Efficient Linkage Mapping Methods for Schistosoma mansoni*	Dr. Timothy J. C. Anderson	2 Yrs.	**$465,267**
NIH/Northshore Hospital/University of Chicago *Gene Expression in an African American Schizophrenia Dataset*	Dr. Harald H. H. Goring	4 Yrs.	**$447,712**
Defense Threat Reduction Agency/University of Texas-Austin *Predictive and Adaptive Responses to Emergent and Engineered Biothreats*	Dr. Robert Davey	2 Yrs.	**$400,402**
NIH/Luminex Corporation *Systems for Rapid Development of High Sensitivity Multiplex Assays for Biothreat Agents*	Dr. Robert Davey	1 Yr.	**$338,029**
NIH/University of Maryland *SOLAR-Eclipse Computational Tools for Imaging Genetics*	Dr. John Blangero	3 Yrs.	**$237,460**
NIH/University of Iowa *Filoviral Glycoprotein/Cellular Protein Interactions*	Dr. Robert Davey	5 Yrs.	**$215,996**
U.S. Army *Feasibility of Lower Body Negative Pressure as a Hypovolemia Model in Baboons*	Dr. Robert E. Shade	1 Yr.	**$201,898**
NIH *Receptor Trafficking in Entry of Murine Leukemia Viruses*	Dr. Robert Davey	1 Yr.	**$188,406**
NIH *Nanoparticle Analysis of Enveloped Virus Entry Pathways (Transfer, NCE)*	Dr. Robert Davey	2 Yrs.	**$159,977**

2012 NEW GRANTS AND CONTRACTS AWARDED

FEDERAL RESEARCH GRANTS AND CONTRACTS	PRINCIPAL INVESTIGATOR	LENGTH	TOTAL AMOUNT TO TEXAS BIOMED
Defense Threat Reduction Agency/University of Texas-Austin *Predictive and Adaptive Responses to Emergent and Engineered Biothreats*	Dr. Robert Davey	2 Yrs.	**$100,000**
NIH/University of Texas Health Science Center San Antonio *Nutrient Restriction: Placental and Fetal Brain and Renal Outcomes and Mechanisms*	Dr. Karen Rice	1 Yr.	**$82,359**
NIH *30th Annual Symposium on Nonhuman Primate Models for AIDS*	Dr. Thomas Folks	1 Yr.	**$75,000**
U.S. Army *Feasibility of Lower Body Negative Pressure as a Hypovolemia Model in Baboons*	Dr. Robert E. Shade	1 Yr.	**$62,400**
NIH/University of Texas Health Science Center San Antonio *Effects of Rapamycin on Small, Short-Lived Primate, the Common Marmoset*	Dr. Kathleen M. Brasky	1 Yr.	**$50,050**
NIH/Baylor College of Medicine *Improving the Safety and Efficacy of Gene Therapy with HDAd*	Dr. Karen Rice	1 Yr.	**$40,000**
NIH/Texas Tech University *Population-Based Mapping of Schizophrenia Genes*	Dr. John Blangero	7 Mos.	**$14,934**
NIH/University of Texas San Antonio *Effects of Aging on Evoked Otoacoustic Emissions in the Common Marmoset*	Dr. Kathleen M. Brasky	6 Mos.	**$3,000**
NIH *Large-Scale Methylation Profiling in Metabolic Syndrome Phenotypes*	Dr. Melanie Carless	5 Yrs.	**$1,500**

TOTAL FEDERAL RESEARCH GRANTS AND CONTRACTS $27,425,162

ACADEMIC RESEARCH GRANTS AND CONTRACTS	PRINCIPAL INVESTIGATOR	LENGTH	TOTAL AMOUNT TO TEXAS BIOMED
Battelle National Biodefense Institute *Efficacy Evaluation in Hartley Guinea Pigs and Nonhuman Primates of a Virus-like Particle (VLP) Filovirus Vaccine in Two Adjuvants*	Dr. Jean L. Patterson	2 Yrs.	**$2,237,738**
Baker IDI Institute *Exome Sequencing-Mauritius Project*	Dr. Joanne Curran Dr. John Blangero	1 Yr.	**$190,000**
Institute for Integration of Medicine & Science - UTHSCSA *Development of a Novel HIV Vaccine Approach Using Chimeric SIV/Varicella Virus*	Dr. Marie-Claire Gauduin	1 Yr.	**$49,894**
Hamada University School of Medicine *Targeted Apoptosis of Peritoneal Endometriosis*	Dr. Robert E. Shade	1 Yr.	**$46,641**
Hamada University School of Medicine *Targeted Apoptosis of Peritoneal Endometriosis*	Dr. Robert E. Shade	1 Yr.	**$13,847**
Baylor Research Institute *Reversal of STZ-Induced Diabetes Using Ultrasound Destruction of Microbubbles for the Delivery of Genes to the Baboon Pancreas*	Dr. Anthony Comuzzie	1 Yr.	**$10,438**
Emory University *Luminex Assays*	Dr. Luis D. Giavedoni	1 Yr.	**$10,211**
University of Texas Health Science Center San Antonio *Preclinical Study of a Neuroprotective Therapy for Parkinson's Disease in Nonhuman Primates*	Dr. Kathleen M. Brasky	8 Mos.	**$8,142**
Baylor College of Medicine *Age-related Retina Degeneration*	Dr. Karen Rice	1 Yr.	**$3,486**
New England Primate Research Center *Luminex Assays/NEPRC*	Dr. Luis D. Giavedoni	1 Yr.	**$3,294**

TOTAL ACADEMIC RESEARCH GRANTS AND CONTRACTS $2,573,691

2012 NEW GRANTS AND CONTRACTS AWARDED

PHILANTHROPIC RESEARCH GRANTS	PRINCIPAL INVESTIGATOR	LENGTH	TOTAL AMOUNT TO TEXAS BIOMED
Wellcome Trust/Drugs for Neglected Diseases Initiative *Validity of PCR and Other Biomarkers for Assessing Parasitological Cure in Chagas Disease*	Dr. John L. VandeBerg	5 Yrs.	**$2,063,591**
Max & Minnie Tomerlin Voelcker Fund (Young Investigator) *Progenitors Derived from Embryonic Stem Cells for Cardiovascular Repair*	Dr. Qiang Shi	3 Yrs.	**$450,000**
Gates Foundation/University of Oxford *Identifying a Laboratory Marker of Artemisinin Resistance*	Dr. Timothy J. C. Anderson	3 Yrs.	**$142,041**
Gates Foundation/Oregon Health & Science University *Polidocanol Foam: Female Nonsurgical Sterilization in a Backpack*	Dr. Karen Rice	2 Yrs.	**$110,000**
Douglass Foundation *Postdoctoral Fellowship*	Dr. Olena Shtanko	2 Yrs.	**$109,620**
Cowles Memorial Trust *Cowles Fellowship*	Dr. Marcio de Almeida	1 Yr.	**$56,619**
Cowles Memorial Trust *Cowles Fellowship*	Dr. Jennifer Neary	1 Yr.	**$56,619**
William & Ella Owens Medical Research Foundation *Development of Potential Response to Radiation Phenotypes (RRPs) for Genetic Studies: A Pilot Study*	Dr. Ravindranath Duggirala	1 Yr.	**$35,000**
Texas Biomedical Forum *Cancer Therapeutic Based on Llama Antibody Guided Bacteria*	Dr. Andrew Hayhurst	1 Yr.	**$35,000**
Joe and Jessie Crump Foundation *Advancing the Models for Liver Cancer*	Dr. Robert E. Lanford	1 Yr.	**$35,000**
William & Ella Owens Medical Research Foundation *Developing a Dual Function Nanosensor for Early Detection of Cancer Cells and Targeted Delivery of Chemotherapeutics*	Dr. Hareesh B. Nair	1 Yr.	**$35,000**
Texas Biomedical Forum *Investigations of Alphaherpesviruses-encoded MicroRNA's during Viral Latency*	Dr. Anthony Griffiths	1 Yr.	**$35,000**
Texas Biomedical Forum *Generation of Neurological Cell Lines for the Study of Bipolar I Disorder*	Dr. Melanie Carless	1 Yr.	**$34,601**
William & Ella Owens Medical Research Foundation *The Osteochondral Interface in Early Osteoarthritis*	Dr. Lorena M. Havill	1 Yr.	**$32,110**
William & Ella Owens Medical Research Foundation *Fine Mapping of Contact Sites within the Ebola Virus Nucleoprotein*	Dr. Daniel A. J. Mitchell	1 Yr.	**$27,734**
Wenner Gren Foundation *Persistent Tanning as a Novel Adaptation to Ultraviolet Radiation in Indigenous Americans*	Dr. Ellen Quillen	1 Yr.	**$25,000**
Faye L. & William L. Cowden Charitable Foundation *Assessing Transcriptional Profiles of the Decidua in Preeclamptic and Non-preeclamptic Pregnancies*	Dr. Matthew Johnson	1 Yr.	**$10,000**
TOTAL PHILANTHROPIC RESEARCH GRANTS			$3,292,935

TOTAL FEDERAL RESEARCH GRANTS AND CONTRACTS	$27,425,162
TOTAL ACADEMIC RESEARCH GRANTS AND CONTRACTS	$2,573,691
TOTAL PHILANTHROPIC RESEARCH GRANTS	$3,292,935
TOTAL COMMERCIAL RESEARCH GRANTS AND CONTRACTS	$2,140,969
TOTAL GRANTS AND CONTRACTS AWARDED TO TEXAS BIOMED IN 2012	$35,432,757

YOUR CONTRIBUTION – INVESTING IN LIFE

EACH AND EVERY DAY, INDIVIDUALS, FAMILIES, FOUNDATIONS AND CORPORATIONS FROM SAN ANTONIO, ACROSS TEXAS, AND AROUND THE UNITED STATES AND THE GLOBE DECIDE TO CONTRIBUTE TO TEXAS BIOMED. THROUGH INVESTMENTS LARGE AND SMALL, THEY SUPPORT EVERY FACET OF TEXAS BIOMED, FROM UNLOCKING THE MYSTERIES OF THE GENES THAT PLAY A KEY ROLE IN SOME OF HUMANKIND'S MOST VEXING DISEASES, TO RESEARCH IN DEVELOPING VACCINES TO PROTECT AGAINST RAVAGING INFECTIONS, AND EVERY AREA IN BETWEEN. THEIR PHILANTHROPY REPRESENTS ALL TYPES OF GIVING, INCLUDING SUPPORT FOR INNOVATIVE PILOT STUDIES, INVESTING IN RECRUITING NEW RESEARCHERS, AND FUNDING NEW LABORATORIES.

Brightest minds.

People who give to support innovative biomedical research do so because they see it as the best possible way to invest in the future. People give to Texas Biomed because they believe it's a place where the donor gets the best possible return on that investment. Unlike some research organizations, Texas Biomed does not have patient or tuition revenue to fund capital and operating expenses. Over time, each donated dollar, on average, has led to $12 of competitive research funding, an impressive return on a donor's investment.

Investing in life.

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

Enhancing life.

When you give, you're part of a visionary group, one that is allowing scientists at Texas Biomed to take on our most intractable health problems. Basic research is an investment in the future. The vision of our founder, Tom Slick, was that innovative research will improve the health of generation after generation. Like Tom Slick, every donor to Texas Biomed has a similar vision.

For more information about any of these giving opportunities, please contact Texas Biomed Vice President for Institutional Advancement, Corbett Christie, at **210-258-9870** or **cchristie@TxBiomed.org,** or visit our website at **www.TxBiomed.org** and click on **"Support Texas Biomed."**

You, too, can make a difference.

TEXAS BIOMEDICAL FORUM

THE FORUM HAD ANOTHER GREAT YEAR IN 2012. WITH THE ANNUAL GALA, STUDENT TOURS, SCIENCE EDUCATION AWARDS, LECTURE LUNCHEONS, SPECIAL EVENTS AND MORE, WE'VE BEEN BUSY PROVIDING OUR 400 MEMBERS WITH OPPORTUNITIES TO EDUCATE, LEARN, SOCIALIZE AND, MOST IMPORTANTLY, TO SUPPORT THE TEXAS BIOMEDICAL RESEARCH INSTITUTE.

We kicked off the New Year with a special event on February 1 at Neiman Marcus in tribute to the spring gala's theme, "Diwali, A Festival of Lights." Guests enjoyed cocktails and light appetizers while being entertained with a runway show featuring evening gowns for spring. All proceeds from the event benefited the Forum.

The annual spring lecture luncheon in March featured Jean Patterson, Ph.D., chair of the Department of Virology and Immunology at Texas Biomed. Her topic, "In the Age of Biodefense," gave guests some insight into the studies that are conducted in the Institute's biosafety level 4 maximum containment lab, which supports our country's biodefense efforts.

Also during this luncheon, winners of the Science Education Awards were announced. The awards are presented annually to local high school teachers who submit the most innovative proposals showing a strong commitment to furthering the development of meaningful science education programs. Given jointly by the Forum and the V.H. McNutt Memorial Foundation, a total of $20,000 in awards was granted this spring. The L.D. Ormsby Foundation also supports the science awards by funding a stipend to all applicants.

One of the Forum's most anticipated events, the annual gala, was held on May 5. "Diwali, A Festival of Lights" transformed The Argyle into a brilliant, festive, and colorful India, dazzling the sold-out crowd of almost 600 and raising $100,000 in seed grants for Texas Biomed scientists. As a direct result of these Forum grants over the years, Texas Biomed has been awarded more than $25 million dollars in larger, federal grants in the last 10 years alone. A list of this year's recipients and their research can be found on page 33 of this report.

Also in May, Suzanne Dabbous, M.D., the Forum's 42nd president, handed over the gavel. Suzanne, a radiologist by profession, in addition to being a wife, mother and philanthropist, was a fantastic and dedicated leader of the Forum last year. The Forum has been fortunate to have Suzanne serve as a trustee in many capacities for the last seven years, as she worked tirelessly to improve our efficiency and continued success.

The Forum returned in the fall with 11 new trustees and 23 continuing their three-year terms. Our first event of the fall was a fall fashion preview runway style show and lunch hosted by Julian Gold in September. In addition to giving us a portion of the

proceeds from the day, Julian Gold stepped it up with a raffle and some fantastic raffle prizes, generating a total of $5,000 for the Forum.

September also marked the kickoff for our annual gala, which will be held on May 4, 2013, at The Argyle. The theme will be "La Gloria Havana" and will celebrate that city's rich culture.

In October we hosted the second annual Roundtable Discussion, a cocktail reception at The Argyle with a panel of scientists from Texas Biomed. This event gave members and guests an opportunity to sit in intimate, rotating groups and learn about current projects and studies under way at Texas Biomed.

Our fall lecture luncheon on November 14 featured Robert Davey, Ph.D., an investigative scientist at Texas Biomed, who presented "Out of Africa: How West Nile Virus and Other African Viruses Impact Our Lives and What We Are Doing to Stop Them."

Also in November, the Forum was chosen as the beneficiary of a special event with Neiman Marcus and renowned jewelry designer David Yurman. Thanks to their generosity, the Forum received a $5,000 gala grant.

Student tours of Texas Biomed in 2012 were at an all-time high. Additional dates have been added for 2013 to accommodate the growing interest from high schools. These tours, coordinated and facilitated by Forum members, give local high school science classes the opportunity to view the impressive facilities at Texas Biomed.

In review, 2012 was another successful year for the Forum, thanks entirely to the countless volunteer hours on the part of many. Now, in the midst of our 43rd year, we look to continue this success in 2013 with opportunities to further our purpose: to support the Texas Biomedical Research Institute through community relations, volunteer service, and fund raising.

Sincerely,

Julie Zacher

JULIE ZACHER,
PRESIDENT, TEXAS BIOMEDICAL FORUM

FOUNDER'S COUNCIL

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."

IN 2012, MORE THAN $38,000 IN GRANTS WAS AWARDED TO THE FOLLOWING SCIENTISTS:

- Tony Comuzzie, Ph.D., for a device to measure biomarkers associated with the pathways for obesity, diabetes, and coronary heart disease.
- Tim Anderson, Ph.D., for a cell counter used in malaria research.
- Lorena Havill, Ph.D., for a device that allows fragile biological samples to be protected from contamination.

TODAY, THE FOUNDER'S COUNCIL — WHOSE MEMBERS RANGE IN AGE FROM 25 TO 46, REFLECTING SLICK'S VISIONARY INITIATIVE TO FOUND THE INSTITUTE AT AGE 25 — INCREASES AWARENESS OF TEXAS BIOMED AND ITS RESEARCH EFFORTS. THE COUNCIL ENCOURAGES WHAT IS HOPED TO BE LONG-TERM PHILANTHROPIC SUPPORT OF THE INSTITUTE, WHILE PROVIDING IMMEDIATE FINANCIAL CONTRIBUTIONS FOR SCIENTIFIC RESEARCH AT TEXAS BIOMED.

In 2012, the Founder's Council hosted two campus tours and three lecture luncheons featuring Texas Biomed scientists. The signature event, "Dining and Discourse," allowed members to participate in lively discussions over dinner with leading researchers. Founder's Council members also enjoyed informal social mixers to network and meet colleagues. Sponsors were secured for all social events in order to maximize support for the Institute.

Members' annual donations of $135 per individual, $195 per couple, and $500 or $1,000 at the Explorer and Adventurer levels of giving, fund competitive grants to Institute researchers for the purchase of key pieces of scientific equipment.

We ended a successful year with 305 members, the largest number in our history. At the holiday party, I had the privilege of presenting an additional check in the amount of $50,000 to Kenneth P. Trevett, president of Texas Biomed, for ongoing research.

These monies signify donations by members at the higher Explorer and Adventurer levels of membership, which were introduced only a year ago. Increasing numbers of people have been signing up at these higher levels of membership, signifying the energy and enthusiasm of the Founder's Council group and, it is hoped, developing a pattern of long-term support that will continue to fulfill Texas Biomed's mission to improve the health of our global community.

Sincerely yours,

Cliff Hurd

CLIFF HURD,
PRESIDENT, FOUNDER'S COUNCIL

- Joanne Curran, Ph.D., for a microplate washer used in tests to characterize disease traits or in studies of complex diseases.
- Robert Davey, Ph.D., for a cell counter used in evaluating the potency of vaccines being tested for Ebola virus and other potential bioterror weapons.
- Anthony Griffiths, Ph.D., for a microscope used to examine the properties of viral cells that can jump from animals to humans to cause disease.
- Andrew Hayhurst, Ph.D., for a centrifuge device to separate components of samples of pathogens and toxins involved in a variety of human diseases.
- Jeannie Chan, Ph.D., for an instrument to replicate small segments of DNA for genetic analysis.
- Melissa de la Garza, Ph.D., for a portable super-pulsed laser to treat nonhuman primates suffering from conditions ranging from bacterial infections to injury.
- John L. VandeBerg, Ph.D., for a microscope to conduct research on Chagas disease.

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Recipients of Founder's Council grants.

THE ARGYLE

FOR MORE THAN 50 YEARS, THE ARGYLE, A HISTORIC SOUTHERN MANSION AND UNIQUE PRIVATE 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 more than 1,400-member club serves as a bond between one of the country's leading independent research institutions 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 famous 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 the members of which 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 Biomed, the club is a meeting place for men and women of science and civic leaders who have dedicated personal resources for the Institute's advancement.

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 a conversational exchange of ideas and information regarding the scientists' research. Argyle members enjoyed four of these "chats" in 2012.

Members were treated to a talk in January by Jean L. Patterson, Ph.D., on "Biodefense Work at Texas Biomed." In March, Matthew Johnson, Ph.D., discussed "Battling High Blood Pressure in Pregnancy." In September, Robert Lanford, Ph.D., kicked off the fall series with a talk titled "Will New Drug Cocktails Provide Hepatitis C Cures for All?" The year was capped off in October by Tim Anderson, Ph.D., who discussed "Malaria Genomics in a Public Health Crisis."

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. ■

TEXAS BIOMED LEADERSHIP

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Cassondra A. Bauer, D.V.M.
Michael A. Owston, D.V.M.

BACK INSIDE COVER: Image shows Ebola viruses entering into human cells by high resolution microscopy. The virus is red, cell nucleus and cytoplasm are blue and lysosomes inside the cell are green.

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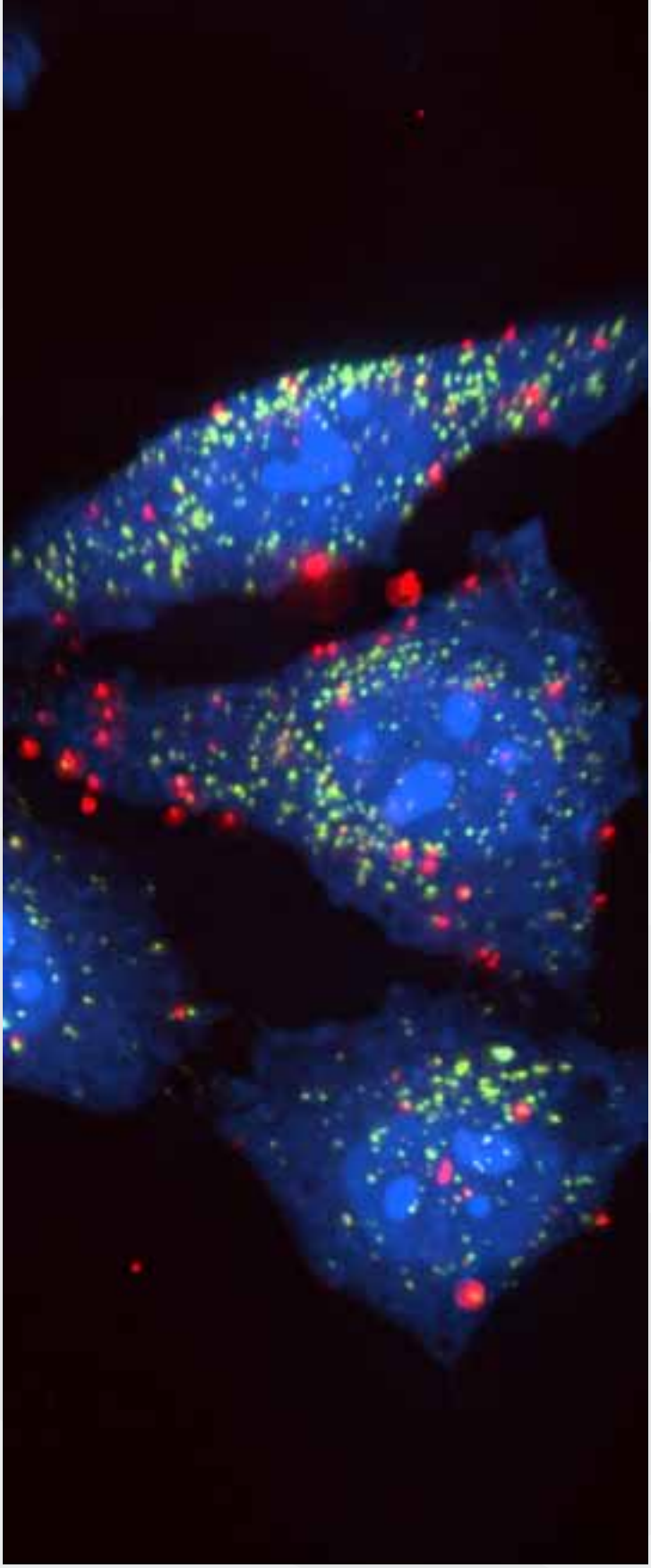

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