



TEXAS BIOMEDICAL RESEARCH INSTITUTE

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Enhancing lives through discoverySM

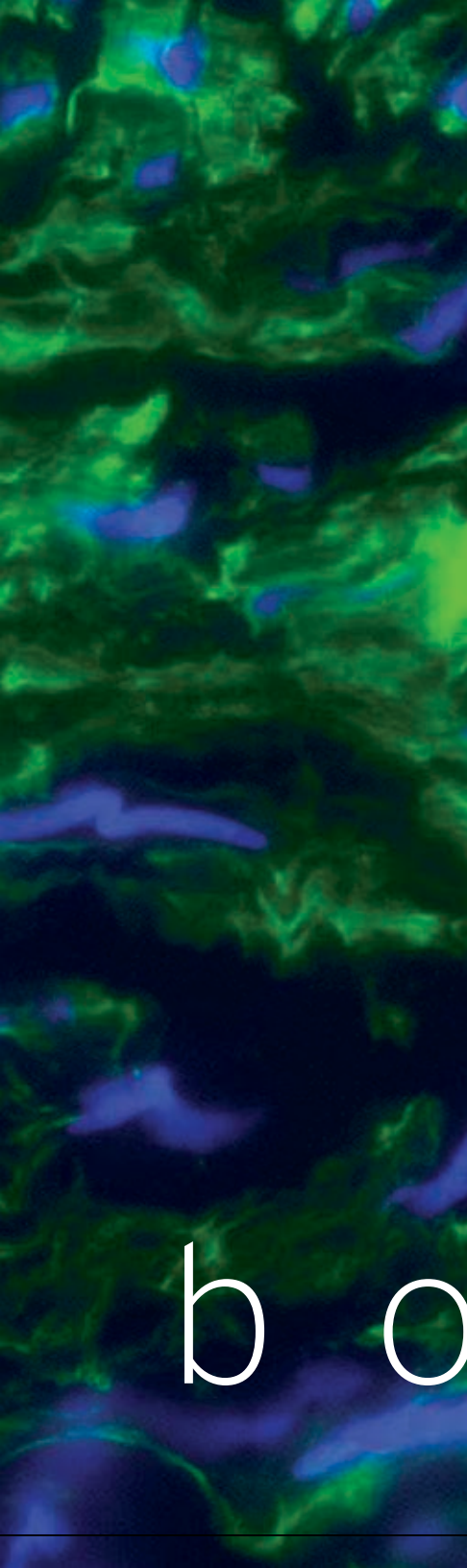
extending boundaries

TEXAS BIOMEDICAL RESEARCH INSTITUTE 2013 ANNUAL REPORT



TEXAS BIOMEDICAL
RESEARCH INSTITUTE

2013
annual report



b o u n d a r i e s



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FRONT INSIDE COVER: Image shows microscopic view of cells that contain alpha-smooth muscle actin stained green, with cell nuclei stained blue. This protein is a marker for cells that constitute the elastic smooth muscle portion of blood vessels. These cells are among the cell types that are being produced in the laboratory from stem cells used to develop artery segments intended for use as replacements for diseased parts of human arteries.

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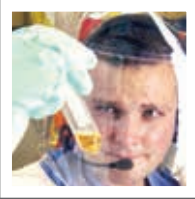


**TEXAS BIOMEDICAL
RESEARCH INSTITUTE**

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BSL-4 LABORATORY

Texas Biomed maintains the only privately owned biosafety level 4 laboratory in the United States



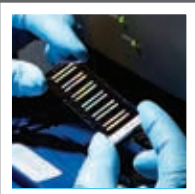
PRIMATE RESEARCH CENTER

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

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 86 DOCTORAL-LEVEL SCIENTISTS WORKS ON MORE THAN 200 MAJOR RESEARCH PROJECTS. USING ITS ONE-OF-A-KIND ASSETS, THE INSTITUTE'S SCIENTISTS ARE DEDICATED TO PIONEERING RESEARCH THAT LEADS TO CURES FOR SOME OF THE WORLD'S MAJOR PUBLIC HEALTH SCOURGES.

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 host to 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 has 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 developed 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 people from the Middle East. Using newly developed statistical genetic methods, a project in Nepal is looking at the genetic components of susceptibility to intestinal worm infections.

Created through the philanthropic vision of Thomas B. Slick Jr. in 1941 and known until recently as the Southwest Foundation for Biomedical Research, Texas Biomed relies on philanthropy to maintain its excellence. Approximately 56 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 two-fifths of Texas Biomed's expenses are met by the generous contributions of foundations, corporations, and individuals, as well as income from Texas Biomed's endowment and royalties.

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

The Texas Biomedical Research Institute is among about 100

INDEPENDENT, NOT-FOR-PROFIT BIOMEDICAL AND BEHAVIORAL RESEARCH ORGANIZATIONS IN THE UNITED STATES. BY BUDGET, WE ARE 10TH IN SIZE, AND BY ENDOWMENT, 6TH. WE ARE THE ONLY SUCH INSTITUTION TO HOST A FEDERALLY DESIGNATED NATIONAL PRIMATE RESEARCH CENTER AND THE ONLY PRIVATE INSTITUTION TO CONDUCT STUDIES IN THE HIGHEST CATEGORY OF BIOLOGICAL CONTAINMENT, BSL-4.

Furthermore, we have the largest collection of computer servers to analyze human and nonhuman primate genomes in the country, if not the world. And our scientific staff is highly regarded internationally for the power of their ideas and the technical capability of evaluating new hypotheses.

What does all this mean? Our independence allows us to be programmatically entrepreneurial and thus be nimble in taking advantage of research and financial opportunities that present themselves. Virtually every visitor to the campus remarks on the disciplined zeal of our investigators and their love of scientific inquiry. Our endowment and oil and gas royalties help sustain our scientific infrastructure and seed new research

initiatives. Our colonies of nonhuman primates enable us to test new hypotheses about the origins of disease as well as new diagnostic, therapeutic, and preventive approaches to life-threatening and life-changing illnesses. Our BSL-4 facility allows us to study deadly diseases for which there are no cures. And our AT&T Genomics Computing Center with 8,000 processors is an essential tool in analyzing billions of bits of genetic data that can lead to new understanding of the heritable factors underlying many diseases.

What is also very important is that Texas Biomed is situated in San Antonio, a city whose clinical and biomedical research institutions are unusually, if not uniquely, collaborative in spirit and deed.

Finally, we have you, our trustees, donors, friends, and fellow researchers, who are committed to the mission of this organization, understand its role in advancing medical care throughout the world, and unselfishly commit time and resources to its betterment. The new Earl Slick Research Center and our two new recruits in Genetics and Virology/Immunology palpably demonstrate the power of the philanthropic community to stimulate change and serve as the foundation for excellence.

This past year was a highly productive year in spite of federal budget constraints, and we anticipate that 2014 will also significantly expand the boundaries of our scientific knowledge. We look to more faculty recruiting, particularly relating to stem cell studies and regenerative medicine, new collaborations with industry, and more emphasis on the transfer of our discoveries to the medical marketplace.

The imperative we embrace is the need to overcome diseases and bio-threats that undermine our well-being and cast a pall on our future and those of the next generation. We have made a difference in human health for nearly 75 years, and with your help and support, we will continue to do so.



Kenneth P. Trevett, J.D.
President and CEO

☒ WE HAVE MADE A DIFFERENCE
IN HUMAN HEALTH *for nearly*
75 years, AND WITH YOUR
HELP AND SUPPORT, WE WILL
CONTINUE TO DO SO.☒

— KENNETH P. TREVETT,
PRESIDENT AND CEO



Texas Biomed scientists in 2013 added another chapter to their impressive

HISTORY OF OUTSTANDING PRODUCTIVITY AND CREATIVITY. THEY MADE MAJOR ADVANCES THAT CONTRIBUTED TO THE INSTITUTION'S MISSION OF IMPROVING THE HEALTH OF OUR GLOBAL COMMUNITY.

During 2013, Texas Biomed researchers published more than 140 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 a heritable basis for neurocognitive degeneration during aging. (*Proceedings of the National Academy of Sciences USA* 110:19006-11, 2013). Identifying the genes that influence the rate of aging will be a first step in delineating the biological mechanisms of aging and developing strategies to reduce the rate of neurocognitive decline.
- Localizing on human chromosome 18, a major gene that influences preterm birth (*Molecular Human Reproduction* 19:687-96, 2013). The gene is likely to be plasminogen activator inhibitor-2, which is active in the placenta. Understanding genetic influences on preterm birth may enable susceptible women to be identified and interventions to be developed.

- Identifying on baboon chromosome 11 a cluster of genes that influence plasma LDL cholesterol levels when the animals are fed a high-fat diet (*Journal of Lipid Research* 54:1776-85, 2013). Understanding genetic influences may lead to new strategies for preventing elevation of plasma LDL cholesterol levels in susceptible individuals.
- Demonstrating that a novel hepatitis B antiviral drug induces prolonged suppression of hepatitis B virus in chronically infected chimpanzees (*Gastroenterology* 144:1508-17, 2013). This is the first novel drug developed in more than a decade for hepatitis B, which kills 600,000 people every year.
- Finding in rhesus monkeys that inflammation of the gums does not enhance oral transmission of SIV, the monkey equivalent of HIV (*Journal of Virology* 87:1750, 2013). This finding indicates that oral transmission of HIV is not likely to be enhanced in people with gingivitis.

- Demonstrating that baboon embryonic stem cells can completely heal an artery that has been stripped of its endothelium, the inner lining that is responsible for the function of the vessel (*Stem Cells and Development* 15:631-42, 2013). This work paves the way for developing bioengineered arteries from human stem cells for bypass operations.

During 2013, Texas Biomed scientists were awarded \$34.6 million in grant and contract funding. Ten 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.

In addition, I express profound appreciation to donors who provided the funding for our new 70,000 square-foot research and scientific support building, scheduled to open in the spring of 2014 and which will house 15 new laboratories. Combined with new scientific recruits, this building will be a major step forward in extending the breadth of research conducted at Texas Biomed and in finding new solutions to solving humankind's most devastating diseases.

Sincerely,



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



☒ DURING 2013, TEXAS BIOMED SCIENTISTS WERE AWARDED \$34.6 MILLION IN GRANT AND CONTRACT FUNDING. TEN 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.* ☒

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



The Earl Slick Research Center

By the end of 2013, the new Earl Slick Research Center

WAS NEARLY COMPLETE AND READY TO BE OCCUPIED. FINISHING TOUCHES WERE BEING APPLIED TO INTERIOR LABORATORIES AND SCIENTIST AND SUPPORT STAFF OFFICES. THE 70,000-SQUARE-FOOT LABORATORY AND OFFICE COMPLEX WAS SURROUNDED BY NEW LANDSCAPING AS BULLDOZERS WERE SMOOTHING THE CONTOURS OF THE REMAINING AREAS BORDERING ON MILITARY DRIVE AND THE I-410 ACCESS ROAD ON THE NORTHWEST SIDE OF THE 200-ACRE CAMPUS.



Betty Slick Moorman, founder of The Argyle, as represented in the Earl Slick Research Center lobby windows.

The \$27 million facility is part of a campus master plan that includes a major effort to recruit world class scientists and to enhance and extend research programs to speed the effort to find the underlying cause and potential treatments for a wide variety of diseases. The recruitment effort includes Robert Davey, Ph.D., and Ruth Ruprecht, M.D., Ph.D., in the Department of Virology and Immunology and Michael Olivier, Ph.D., in the Department of Genetics. Other recruitments are under way, including two researchers in the area of regenerative medicine. All of these efforts enhance Texas Biomed's global impact in developing new pioneering scientific initiatives that lead to cures and promote the translation of discoveries into medical progress. ■

6

additional faculty members in the Genetics and Virology and Immunology departments

2

additional faculty members recruited for the SNPRC

2

additional researchers recruited for a regenerative medicine program

70K

square footage of new laboratories and scientific service space

15

additional research laboratories



Two World Class Researchers
Strengthen Texas Biomed's Capacity
in the Areas of HIV/AIDS Research
and the Screening of Drugs for
Potential Bioterror Threats



The recruitment of two distinguished scientists to Texas Biomed Department

OF VIROLOGY AND IMMUNOLOGY REFLECTS NEW CHALLENGES AND OPPORTUNITIES IN THE FIELD THAT OFFER REAL HOPE FOR OVERCOMING MANY DISEASES, INCLUDING POTENTIAL BIOTERROR THREATS. ROBERT DAVEY, PH.D., SCIENTIST AND EWING HALSELL SCHOLAR, HAS A CREATIVE RESEARCH PROGRAM IN SCREENING THOUSANDS OF DRUGS THAT MIGHT BE REPURPOSED TO TREAT VIRAL DISEASES.

but the other side of the coin is drugs. So to identify new drugs is extremely difficult, and you can't think on a small scale. You have to do big science. My approach is to collaborate with people who have very large drug libraries and to set up systems that allow me to pull out those chemicals that do something to stop the virus. At Texas Biomed, we use state-of-the-art systems to do high throughput screening in the BSL-4, and we probably are the best in the world at that.

Ruth Ruprecht, M.D., Ph.D., scientist and director of the Texas Biomed AIDS Research Program, is a pioneer in the development of AIDS vaccines and the prevention of HIV transmission from mothers to babies. Annual report editor Joseph Carey interviewed Davey, Ruprecht, and Jean L. Patterson, Ph.D., the department chair, on the progress and promise of this research.

Q. Dr. Patterson, how has the department evolved since you first arrived here in 1996?

PATTERSON: There was some hepatitis and some HIV research, and my charge was to rebuild the department. We did a national search, and we brought in people working in emerging diseases and additional HIV research. Then we recruited more HIV researchers and people to work in the biosafety level 4 (BSL-4) laboratory after it opened in 2000. After 9/11, there was a lot of biodefense research funding. At one point, we were a third biodefense, a third hepatitis, and a third HIV. Right now, our concentration is about 10 percent hepatitis and equally divided between HIV and biodefense.

Q. How do these two new scientists complement and add to the department's existing research programs?

PATTERSON: We already have two researchers who work on HIV. Both are interested in pathogenesis and vaccine development, and these areas are Ruth's forte, particularly in transmission. So she complements what the other HIV people are doing. Rob Davey has been a collaborator of ours in biodefense for a number of years, so he was already working with people in the department. He brings antiviral research for biodefense as well as basic research in viral entry — all in the BSL-4.

Q. Dr. Davey, what made Texas Biomed an attractive place for you?

DAVEY: It was two factors: the BSL-4 and Jean. I had collaborated with her and knew that she had a good vision for the department, and I wanted to be a part of that. And the BSL-4, of course, is absolutely fundamental to my work.

Q. How do you approach your research?

DAVEY: For me, I think drugs are the way to go to cure a lot of diseases. Vaccines are very important,

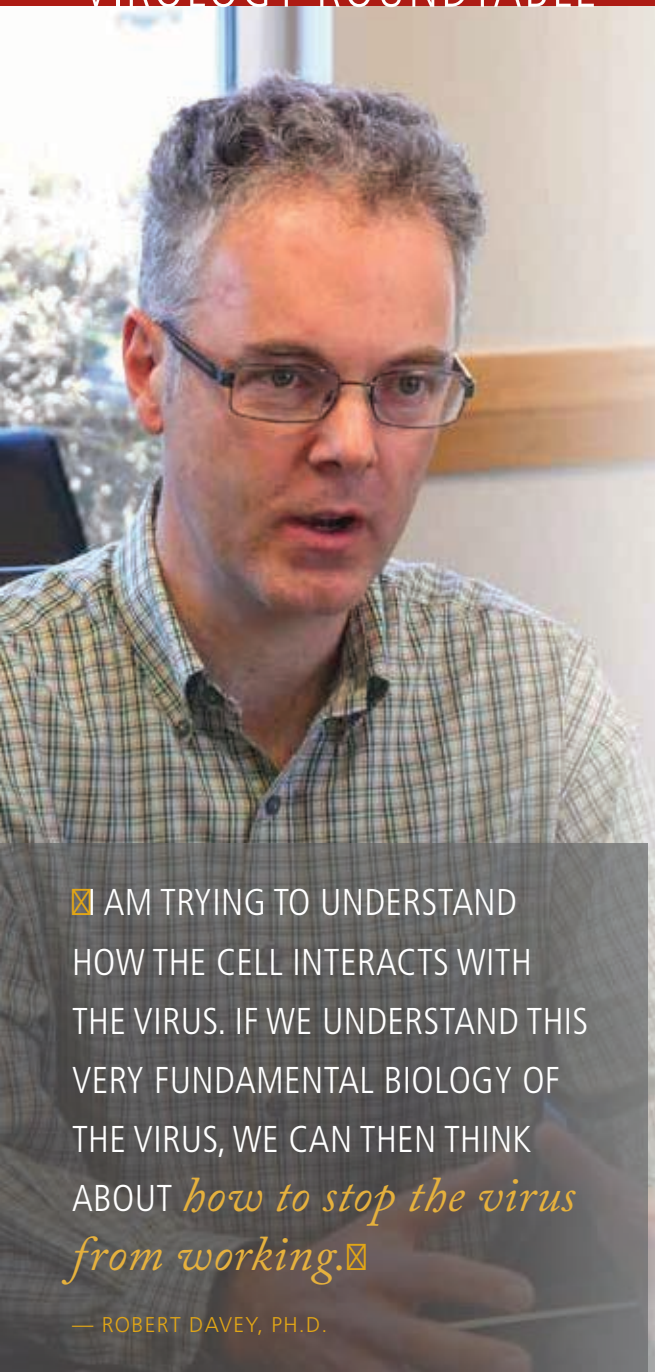
Q. What is the range of viruses that you study?

DAVEY: They are viruses that are of most concern to biodefense and are emerging infectious diseases. These viruses appear almost out of nowhere, and they flare up every year, kill many people, and then disappear again. Ebola virus is one that most people know about. It's actually appearing with increasing frequency every year, mainly in Africa. But we have to be concerned about these things heading in our direction through people who are sick and then hop onto airplanes, appearing at the other end and infecting other people. We want to be prepared for them, but we are really not. Hospitals have quarantine facilities, but it might be too late by the time someone is recognized as having one of these exotic diseases before something is actually done. So, we need vaccines and drugs.

Q. Tell us about some of your recent findings.

DAVEY: I am trying to understand how the cell interacts with the virus. If we understand this very fundamental biology of the virus, we can then think about how to stop the virus from working. We can

Left to right, Jean L. Patterson, Ph.D., Robert Davey, Ph.D., and Ruth Ruprecht, M.D., Ph.D.



☒ AM TRYING TO UNDERSTAND HOW THE CELL INTERACTS WITH THE VIRUS. IF WE UNDERSTAND THIS VERY FUNDAMENTAL BIOLOGY OF THE VIRUS, WE CAN THEN THINK ABOUT *how to stop the virus from working.*☒

— ROBERT DAVEY, PH.D.

get a new drug or chemical that prevents that function inside the cell, and the virus is then crippled. Recently, one of my postdocs, Olena Shtanko, Ph.D., discovered a process called autophagy that is important for Ebola virus. Normally, it's like the garbage removal system of the cell. It turns out that the Ebola virus is actually very dependent on proteins that control autophagy; and when you block some of those proteins, Ebola virus can no longer infect the cell. These proteins are helping the virus get inside the cell. It appears to be a unique aspect of Ebola virus infection that we could use against it.

Another postdoc in my lab, Yasuteru Sakarai, Ph.D., has discovered that a Chinese herbal remedy used to treat high blood pressure also protects mice in the BSL-4 against the Ebola virus infection. This drug seems to block the earliest step of infection, so we are quite excited about this. I think we are getting very close to something that will actually work in the clinic. The next step is to take this research into monkeys, which depends on funding.

Q. *Dr. Ruprecht, for you the primate center was an attractive lure in getting you to join Texas Biomed.*

RUPRECHT: Yes, the primate center has experts in primatology, which is outstanding here. This and the immediate access to primates as well as direct access to cells and tissues from primates is what got us here. My group has been working for 25 years with primates and primate models for HIV and AIDS, but it has always been a long-distance relationship. Our research in AIDS virus transmission and its prevention has made such advances that we decided

we had to be where the expertise was and that we had to be located at the site where the primates were.

Q. *So you work on both AIDS transmission and development of vaccines?*

RUPRECHT: In terms of basic science, we are focusing on very early steps of HIV infection. How does the virus get transmitted? Most of the HIV transmissions happen through mucosal surfaces — whether it's through sexual exposure or through mother-to-child transmission, especially through breast feeding. We are now collaborating with a group that has developed “colored” viruses — viruses that emit fluorescent light. There are green viruses, red viruses, and yellow viruses. With this new technology, we can actually find out how the virus enters the body, how it squeezes through the lining of the various mucosal surfaces, how the first target cells get infected, and what type of cells these are.

We look simultaneously at the role of antibodies. We are studying what antibodies cover the virus particles and whether such antibodies help to prevent or possibly enhance the infection. My group also has a long track record of using passive immunization for prevention. That means giving preformed antibodies to prevent virus transmission. We also have a long track record of developing active immunization. That means giving animals a shot to induce immune defenses directly. Our long-term goal is to combine passive and active immunizations to prevent mother-to-child transmission of the AIDS virus.

Q. *Why has it taken so long to get a vaccine for AIDS?*

RUPRECHT: The virus itself does not induce any protective immunity. An infected person actually can get superinfected with other HIV strains, and with such superinfections, the virus can mutate even more. The main difficulty for getting an AIDS vaccine is that the virus mutates very fast. It's like a moving target. In a chronically infected person, the virus exists in many different versions, so-called strains. So how do you find a vaccine when there are millions and millions of different virus strains out there? What we have to do is find common targets that these millions and gazillions of different virus strains share. This has never been done before.

Q. *So where are you in this search to find something that works?*

RUPRECHT: We are now 30 years beyond the discovery of the AIDS virus. There have been a number of preclinical trials in nonhuman primates and clinical trials in humans, and for many of the years, it was always gloom and doom, especially in the clinical trials. But in 2009, for the first time, there was a glimmer of hope: There was a modestly successful clinical trial, the so-called RV144 trial. It was recently published by researchers from the Thai government and the U.S. Army. For the first time, there was some indication of protection among the vaccinated people, a modest 31 percent. That wasn't enough to bring the vaccine that was tested to the clinic as a standard treatment intervention approach, but at least it showed proof-of-principle that there may be a way of overcoming these very significant hurdles.

PATTERSON: *What was the vaccine platform for that trial?*

RUPRECHT: For the first time it was a combination approach: using two different vaccine strategies at the same time. The initial idea for developing an AIDS vaccine was to develop an antibody-based defense that has worked against other viruses. The idea was that, if you make antibodies against the envelope molecule on the surface of the virus particle, then you block virus entry; the virus can't infect. That didn't work. Because the antibodies didn't work, the pendulum swung all the way to the other side. The thinking was that, since antibody defenses did not protect, maybe a cell-based vaccine would work. So the next idea was to develop a vaccine based only on T-cell defenses.

Q. *So what led to the success of the recent trial?*

RUPRECHT: The reason why the trial in Thailand worked was that, for the first time, two ideas were combined, namely to induce antibodies and T-cells simultaneously. The result of this combination approach surprised everybody. Paradoxically, neither the antibody approach by itself was effective, nor was the T-cell approach. A letter-writing campaign tried to stop this expensive trial that was to enroll two groups of roughly 8,000 people each at a huge expense. But to their credit, the investigators stuck to their guns and carried out the trial. The surprise was that the two components when used together showed some modest protection.

Q. *What are some of the technological advances?*

RUPRECHT: For many years, preclinical and clinical trials in the HIV/AIDS field have really been depressing. But new developments that have advanced the field include the use of viral vectors, molecular cloning, molecular biology approaches, and the ability to do sequencing better and cheaper. That now allows a bioinformatics approach that is revolutionizing the field. The isolation of new monoclonal antibodies from HIV-infected people has been generating the most excitement. These new antibodies have the ability to neutralize and block the majority, if not all, of these millions of different strains of HIV. Neutralization of those strains that have been tested had an impressive efficiency. New technologies have been developed to isolate antibody-producing B-cells from animals or from people. Monoclonal antibodies can then be generated from single B-cells.

My group has developed technologies to isolate very specific memory B-cells from vaccinated rhesus monkeys. In theory, you can give a vaccine to a rhesus monkey that you can't give to people. You can then isolate the antibody-producing cells from the monkey, and with the help of molecular biology and cloning techniques, you can isolate genes that encode the antibodies. This will allow you to generate monoclonal antibodies.

We have developed the technology to make them very specific for targets that warrant them. Combined, these new monoclonal antibody technologies have now shown, at least in principle, that the AIDS virus is

vulnerable, that antibodies can block it, especially if the monoclonal antibodies are used in combination.

We have used triple or quadruple combinations of such anti-HIV monoclonal antibodies; these antibody combinations stopped all viruses from infecting any cells. In monkey trials, we were able to protect all animals from becoming infected by giving them combinations of monoclonal antibodies as prophylaxis. It is now possible to use the new, very potent monoclonal antibodies that have been recently isolated by several groups in combination and to administer passive immunization, as I've mentioned before. By treating with preformed specific molecules, we give the antibodies that block the virus infection.

The fact that about 1 in 2,000 people that carry the AIDS virus actually have made such potent and strong neutralizing antibody responses gives hope that maybe we can figure out with bioinformatics and molecular biology techniques how to induce such antibody responses in everyone with a vaccine.

Q. *Scarce science funding has been an issue for several years, and it doesn't appear to be improving. Apart from that, are there other challenges that your field faces that need to be overcome to develop successful treatments and vaccines?*

PATTERSON: Yes, I think Rob and I — because we work with select agents — face an enormous amount of bureaucracy and



OUR RESEARCH IN AIDS VIRUS TRANSMISSION AND ITS PREVENTION HAS *made such advances* THAT WE DECIDED WE HAD TO BE WHERE THE EXPERTISE WAS AND THAT WE HAD TO BE LOCATED AT THE SITE WHERE THE PRIMATES WERE. ☒

— RUTH RUPRECHT, M.D., PH.D.



☒ THE BEST PEOPLE WILL BRING THEIR AREAS WITH THEM, AND THAT HAS BEEN OUR APPROACH. WE NEED GOOD VIROLOGISTS HERE TO *help us expand our experiments.*☒

— JEAN L. PATTERSON, PH.D.

regulations that can really slow things down. It is just because these things are potential biological weapons, and the government wants to keep a close look at them; and that is always a moving target. So we spend a lot of time making sure that we are not running afoul of these regulations. The regulators are the Centers for Disease Control and Prevention and the National Institutes of Health, and now Homeland Security will be in charge of some agents.

Q. *So are all the agencies on the same page, or are they telling you different things?*

DAVEY: They tell us different things often, but it is really on us to make sure that our people are functioning properly. And that is being pushed more and more onto us to do. I think we do that effectively because we are a small group, unlike some other facilities.

PATTERSON: We all know the person next to us, and we keep our finger on the pulse of what is going on. We know where everything is kept and monitored, and we have very strict regulations within this institution about how we handle select agents.

Q. *Switching topics, San Antonio is known as a place where collaboration is relatively easy to do with other institutions. Please talk about your collaborations with other institutions here.*

DAVEY: The Center for Translation and Science at the UT Health Science Center — they are a large group interested in health issues in the local community. I have been working with their drug screening group.

They have good facilities like we have here, so that's important. Their primary goal is to get things from bench to the bedside. They can bridge me to the clinic, which I can't do by myself. Also, I am working with the Southwest Research Institute's organic chemistry experts who are making new drugs for me.

Q. *What about collaborations abroad?*

DAVEY: I recently spent two weeks in Russia where I am working with their scientists to develop diagnostic tests for some virus infections that are common there. They are building up their biotechnology industry right now, and they need some guidance. They want to know how to get to the next point of bringing things to the clinic; and because we have been thinking about these things for the last 10 years, I can offer some advice. They are particularly worried about tick-borne encephalitis and another virus called Crimean-Congo hemorrhagic fever (CCHF), which is often transmitted quickly within hospitals. I am about to do some work with nonhuman primate models on CCHF, and that hopefully will be the first animal model for that virus.

We are giving them a diagnostic system that allows them to detect the virus antibodies without actually having to use the virus itself. With a lot of diagnostic systems, you need to first grow the virus, put it onto a plate, and then do the test. For the viruses that the Russian scientists are concerned about, these really need to be grown only in a BSL-4 lab. So there is a lot of risk in doing the diagnostic assay. Instead, we are giving them a system that doesn't have to

work with the dangerous bug anymore. This, of course, decreases the risk to clinical lab workers by preventing accidental exposure.

RUPRECHT: I have been collaborating with the People's Republic of China for a number of years. In 2001, I was asked by the China Center for Disease Control and Prevention to help them evaluate their primate centers and to co-write a grant application to the U.S. Government for the Comprehensive International Program of Research on AIDS. Under this program, I was sent to different primate centers in China and realized that they had tremendous numbers of animals and resources but that their facilities were not up to standards. So I advised them on major renovations, introducing proper biocontainment, and training of personnel. I have gone back to China once or twice a year ever since.

Q: *Dr. Patterson, please talk a little bit about the future of the department and its research areas.*

PATTERSON: The best people will bring their areas with them, and that has been our approach. We need good virologists here to help us expand our experiments. Ruth and Rob are very good virologists. Viruses have a lot more in common with each other than not, and so with everyone coming in with a good solid knowledge of virology, it will create a positive effect for everybody's research program. Everyone's expertise with their particular virus can be used in their colleagues' programs. ■

Dick Schlosberg, Former Newspaper Publisher, Becomes New Texas Biomed Board Chair

Nattily attired in a blue dress shirt and red

TIE, DICK SCHLOSBERG SITS AT A CONFERENCE ROOM TABLE FOR AN INTERVIEW. HE SIPS A CUP OF BLACK COFFEE WHILE AN ELECTRONIC RECORDING DEVICE HOOKED UP TO A LAPTOP COMPUTER CAPTURES THE CONVERSATION.

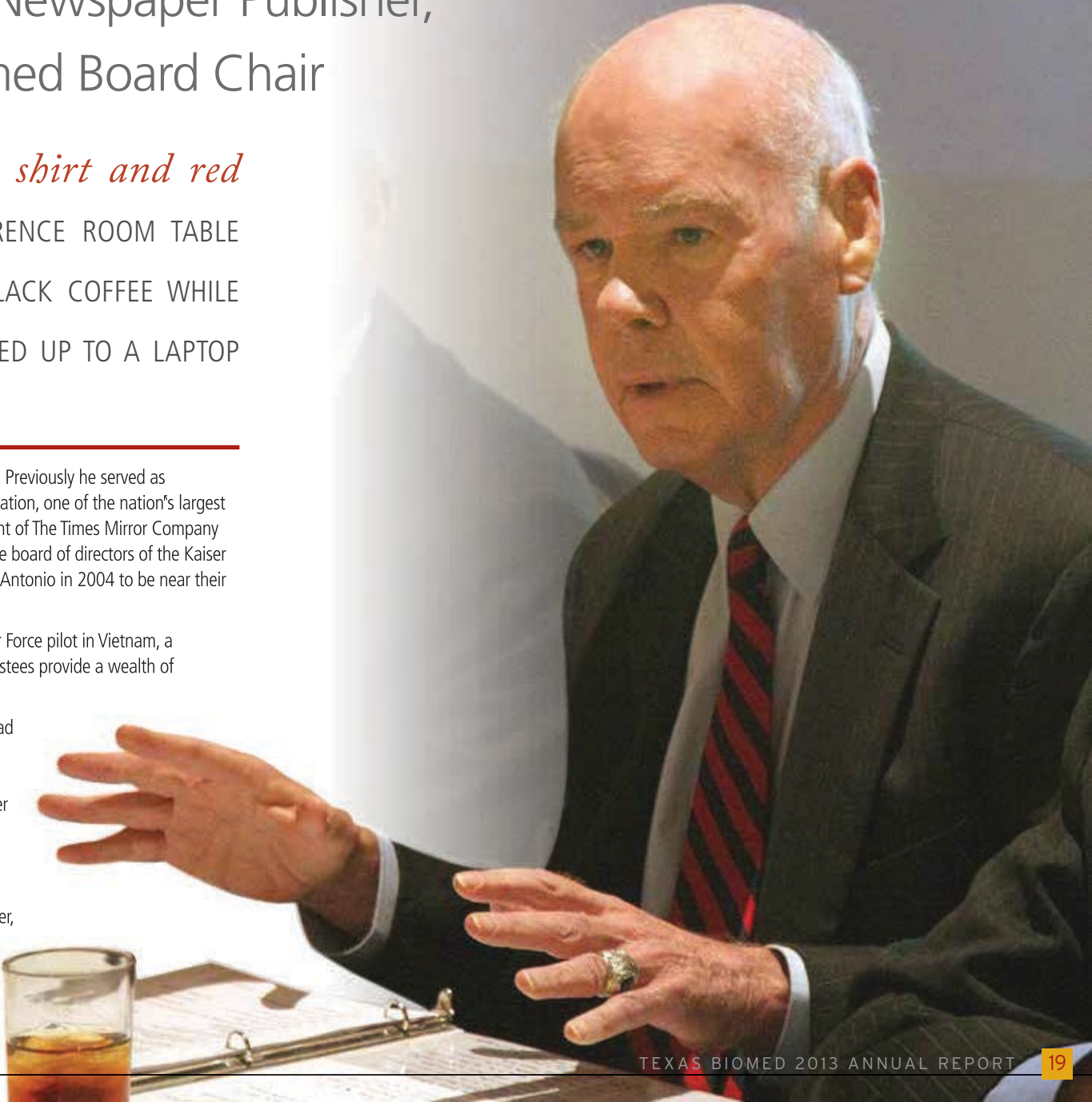
Schlosberg became chair of Texas Biomed's board of trustees in June 2013. Previously he served as president and chief executive officer of the David and Lucile Packard Foundation, one of the nation's largest foundations. Before joining Packard, Schlosberg was executive vice president of The Times Mirror Company and publisher and CEO of the *Los Angeles Times*. He is also chairman of the board of directors of the Kaiser Family Foundation. He and his wife, Kathy, moved from Los Angeles to San Antonio in 2004 to be near their son, daughter and grandchildren.

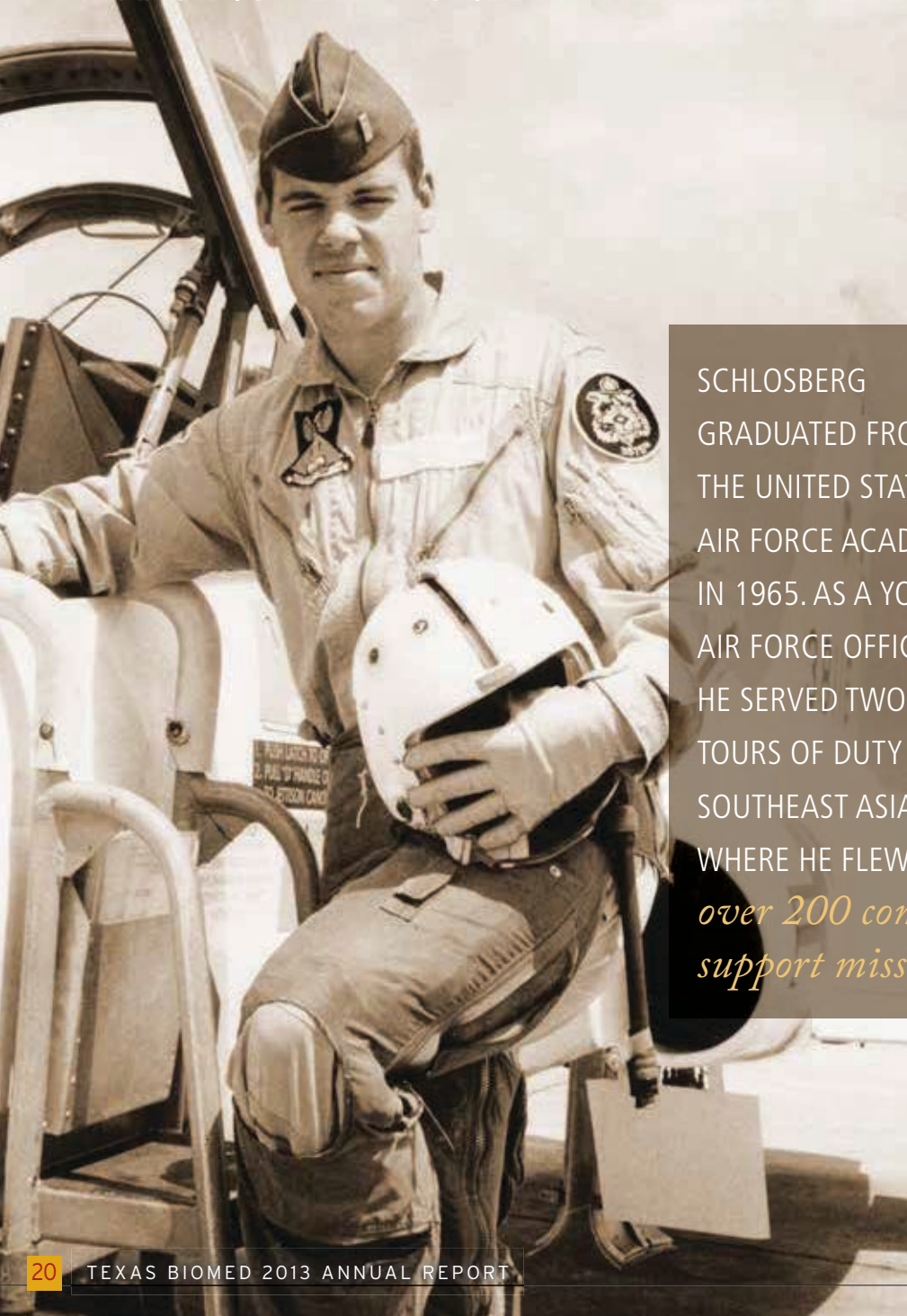
His experiences growing up in a constantly moving military family, as an Air Force pilot in Vietnam, a publisher of several major newspapers, and chair of nonprofit boards of trustees provide a wealth of knowledge very relevant to his new position at Texas Biomed.

"We are extremely fortunate to have Dick Schlosberg — with whom I've had the pleasure of working closely in several other San Antonio enterprises — leading the Texas Biomed board of trustees," said John Kerr, a former Texas Biomed board chair. "His board experience and leadership roles at a number of leading national corporations and nonprofits will be exceptionally valuable as we continue to build Texas Biomed into one of the leading independent research institutes in the United States," he added.

Gazing intently across the table, Schlosberg discusses his personal life, career, and role as board chair.

A robust and fit 69, Schlosberg has been a passionate runner for 36 years. He was featured in *Runner's World Magazine* in 1994 and has three New York marathons to his credit. It all started when he checked





SCHLOSBERG GRADUATED FROM THE UNITED STATES AIR FORCE ACADEMY IN 1965. AS A YOUNG AIR FORCE OFFICER, HE SERVED TWO TOURS OF DUTY IN SOUTHEAST ASIA WHERE HE FLEW *over 200 combat support missions.*

himself into the Cooper Clinic in Dallas at age 33, worried about his risk for heart disease because his father passed away at age 55 from a heart attack.

He calls running energy-replenishing, which is why he runs in the early morning both indoors and out. "I can enter a deep "Zen" on a treadmill," he said, "while I'm listening to Bruce Springsteen, Bob Seger and Elton John."

EARLY LIFE

Schlosberg was born in 1944 in Ardmore, Okla., where his father was stationed in the Army Air Corps. He grew up in Germany, France, Spain, and Alexandria, Va. He skipped his junior year and graduated high school in Seville, Spain. At age 17, he was the youngest in his U.S. Air Force Academy class. He graduated in four years and in 1965 married Kathy, whom he first met in Germany before high school.

After five years in the Air Force and flying more than 200 combat support missions in Vietnam refueling fighters and bombers in the combat zone, he decided to enter civilian life. This was a "big deal" for someone from a military career family, he recalled.

"Kathy said: "What are we going to do?" I said: "I don't know."

The first stop was Harvard Business School, but he wanted to do something different from being a product or financial manager.

"I needed to have something that had not just a business component to it, but a social responsibility

element that had a bigger cause than the bottom line," he said. "So I took a gamble and became business manager of a 50,000-circulation newspaper in Anderson, S.C.

PUBLISHING CAREER

"Mine was a day job, but reporters came in during the afternoon and they went out late. So I would stay and be a copyboy. I was the number two guy at the paper, but I switched gears. The lesson was that there are no small jobs. You can learn from everything if you keep your eyes open, and so I learned a lot about how journalism works and its values — the difficulty of the often quoted "the best truth you can come to quickly," the first draft of history. I saw people trying to get it right."

Schlosberg tries to be mindful of the importance of humility and staying grounded. As publisher of the *Denver Post*, he remembered one time when that adage got away from him.

"When I found out in 1993 that I was going to be the publisher of the *Los Angeles Times*, I came home that night and during dinner with Kathy, I said, "Do you realize how many important publishers there are in this country?" And she said, "Well no, but there is one less than you are thinking." I said: "Good point."

And now, with all the changes in print journalism since the advent of the digital age, where does he think the field is headed?

"The future of the newspaper product, ink on newspaper, is dim," Schlosberg said, "and that's okay with me. What I am concerned about is the future of journalism. The fundamental watchdog role of newspapers is essential to freedom and democracy. When you travel around the world as Kathy and I have, both at the *LA Times* to all our bureaus, and later at the Packard Foundation, you really see that freedom without freedom of the press is not real freedom. It is essential for people

to have a press that speaks truth to power and is free to practice. I'm not optimistic that there will be a business model of ink on paper that is going to be sustained, but I am hopeful that there will be some business models that would give journalism a platform it needs to perform its craft. That to me is the big concern.¹⁵

WHY TEXAS BIOMED?

Turning to his latest concern and new position as Texas Biomed board chair, Schlosberg recounted how he came to recognize the importance of basic research. The Packard Foundation funded basic research at a high level based on the belief that it was the key to progress, he said.

"So I became a fan of giving bright people resources and getting out of their way. I love that model, and that's the appeal of Texas Biomed along with the people associated with it," he added.

When the idea of the trustees' chair was first suggested to him, Schlosberg said he was not available because of his many other board responsibilities on the West Coast. But then he saw that he had some "off ramps" that were going to give him the time he needed.

"I had not intended or expected to be in a leadership position quite this early, having joined the board as a trustee in 2010.¹⁶

Now is an exciting time for Texas Biomed, he said.

"All of the trustees are very proud of the work done here and it is truly a privilege to be associated with the organization and a privilege to lead the trustees.¹⁷

BOARD CHAIR

One of Schlosberg's first tasks was to conduct a series of "get to know you" interviews with scientific and administrative leadership so that he fully understands Texas Biomed and can "be sure

that all the good that has happened here can be maintained and improved on.¹⁸

The chair needs to have a constructive working relationship with the CEO, he said. The chair should also be a resource for the CEO and senior management to consult and be available.

"Another part of my job is to ensure that the board is engaged and that we are set up in a way that will allow each board member to contribute in a way that is comfortable for him or her.

"I always say to all of the boards that I have been associated with that we want to upgrade the gene pool, which should be easier here, shouldn't it? After all, we have a whole department devoted to genetics. We have a great board, but you always want to look for ways to improve its effectiveness and get it engaged in some of the bigger strategic issues facing Texas Biomed, such as the challenges resulting from reduced funding from the National Institutes of Health," Schlosberg said.

He firmly believes that effective boards know the difference between management and governance.

"We look to management to manage and lead. We as board members look to consult and to govern. It sounds trite, but good boards show up and are involved. They also are excellent representatives in their various communities, whether it's the local community or their professional community, and they represent the institution.

"They are involved in the development process in a way that is comfortable for them. A lot of people think that development is asking for money, but that is just one of the steps for development. There are also friend-making and making people aware. We want to continue to see the board's effectiveness improve, and I think that we have a great base to build on here. The board has been excellently led by J.R. Hurd, John Kerr, and their predecessors.¹⁹

RECRUITING A CRITICAL MASS

Schlosberg says it's too early to count specific goals for his term because he is still in his "orientation stage."²⁰ But one goal he is certain of is continuing to recruit world class scientists.

"It's like building a newspaper in that you attract a few great people and then other great people want to be there," he said. "It is a critical mass that forms, and we already have a distinguished group here that I hope to build on."²¹

As a board member of eBay since 2004, Schlosberg has a contemporary perspective on how to boost the recruiting effort and make Texas Biomed known more broadly and in new ways.

"We need to harness the power of mobility, social media, and digital communications in a way that makes sense, that fits this institution," he said. "That is going to be important for us. It's a matter of having a different window on how people consume and digest information and communicate with each other, and it's segmenting the market. So I think that we have to feel our way and find out what's right for us, and we probably need to have some people around us who think differently than we do.

"I have a mentor at eBay who's 26 years old, and I think a lot of us would be well served to be mentored by a younger person who lives in a different kind of information consumption life than we do," Schlosberg said. "It's far different. Kids do thousands of texts. I can talk to my granddaughters, and they are talking to me and having a conversation while they are texting. The thumbs are at a different place in their brain. So I think it will be a challenge for us, but I am excited about that challenge. I want to help us get there."²²

By now nearly 60 minutes have passed. The coffee cup is empty. A final question ponders how someone who obviously has been through very tense situations throughout life can appear so calm and composed. Who is the inner Dick Schlosberg?

GUIDING PHILOSOPHY

"When you are 25 years old and you have friends who are killed or become POWs you will learn about adversity," he said. "When you really learn at an early age that the best things in life are free, it's very liberating, and it gives you great freedom and inner calmness about dealing with other issues in your life.

"So when business or personnel crises happen to me, in all frankness they don't rattle me, because I know what being rattled is like. It's just business, and I think I have a very good perspective on what's really important, and what real adversity is. My Southeast Asia experience sort of set a stage for my business life and orientation, which has been very helpful."²³

With this line of thinking, Schlosberg recited from memory part of the Rudyard Kipling poem *If*, which starts: "If you can keep your head when all about you are losing theirs and blaming it on you, If you can trust yourself when all men doubt you, But make allowance for their doubting too. . . ."²⁴

Schlosberg added: "I try to live that, but don't mistake an easygoing nature for lack of determination or commitment to get the job done." ■

Mexican American Youth Show Signs of Metabolic Syndrome

Childhood obesity and associated cardiometabolic

RISK FACTORS HAVE BECOME MAJOR PUBLIC HEALTH ISSUES IN THE UNITED STATES, AND THEY DISPROPORTIONATELY AFFECT ETHNIC MINORITIES, INCLUDING MEXICAN AMERICANS.



Mexican American children were found in a recent study to be experiencing substantial burdens of obesity, prediabetes, and other health problems that historically would have been expected to develop much later in life.

The findings of a new study by Texas Biomed scientists argue for early screening and intervention to delay or avoid chronic health problems as these children age.

Results of the study, directed by Texas Biomed scientist Ravindranath Duggirala, Ph.D., in collaboration with scientists from the University of Texas Health Science Center at San Antonio and other institutions, were published in the journal *Human Genetics*. The research was funded primarily by the National Institute of Child Health and Human Development, a division of the National Institutes of Health (NIH).

Metabolic syndrome is a cluster of early warning signs for diabetes, heart disease,

and other major medical problems. These warning signs, or cardiometabolic risk factors, include increased accumulation of fat around

the waist and in the blood as well as elevated blood pressure and blood sugar and high insulin levels. An estimated 2.5 million adolescents in the United States have metabolic syndrome, with minority groups such as Mexican Americans being particularly vulnerable.

INCREASED BURDEN OF METABOLIC SYNDROME

This new study examined 670 nondiabetic boys and girls, between the ages of 6 and 17 years, from predominantly lower-income extended Mexican American families, many of whose adult members have increased risk of diabetes. The study found that nearly 53 percent of the children were overweight or obese, and 13 percent had prediabetes. Overall, 19 percent — almost one in five — of the young people exhibited metabolic syndrome. The prevalence of metabolic syndrome rose dramatically with increasing

obesity, and among 65 severely obese young people in the study, more than two-thirds had already developed the condition.

The young study participants were all enrolled in the San Antonio Family Assessment of Metabolic Risk Indicators in Youth (SAFARI) study and went to the Texas Diabetes Institute for the clinic examinations associated with the project. Because all the children belonged to families whose adult members had previously participated in genetic studies led by Texas Biomed and the Health Science Center, the researchers were able to draw upon extensive family information to identify strong evidence of heritability for the metabolic syndrome and its related traits.

EARLY SCREENING

The ultimate goal of SAFARI investigators' efforts is to find better ways to prevent or delay disease. "Much attention has been devoted to environmental and lifestyle contributors to obesity," said Duggirala, SAFARI principal investigator. "But these data provide insights into the complex genetic architecture underlying risk for cardiometabolic disease in these children. Insights gained through a genetic approach may help to tailor effective dietary, physical activity and other interventions for high-risk young people."

INSIGHTS GAINED THROUGH A GENETIC APPROACH MAY HELP TO TAILOR EFFECTIVE *dietary, physical activity and other interventions* FOR HIGH-RISK YOUNG PEOPLE.™

— RAVINDRANATH DUGGIRALA, PH.D.

» The Dangers of Metabolic Syndrome

Mexican American children were found in a recent study to be experiencing substantial burdens of obesity, prediabetes and other health problems that historically would have been expected to develop much later in life.

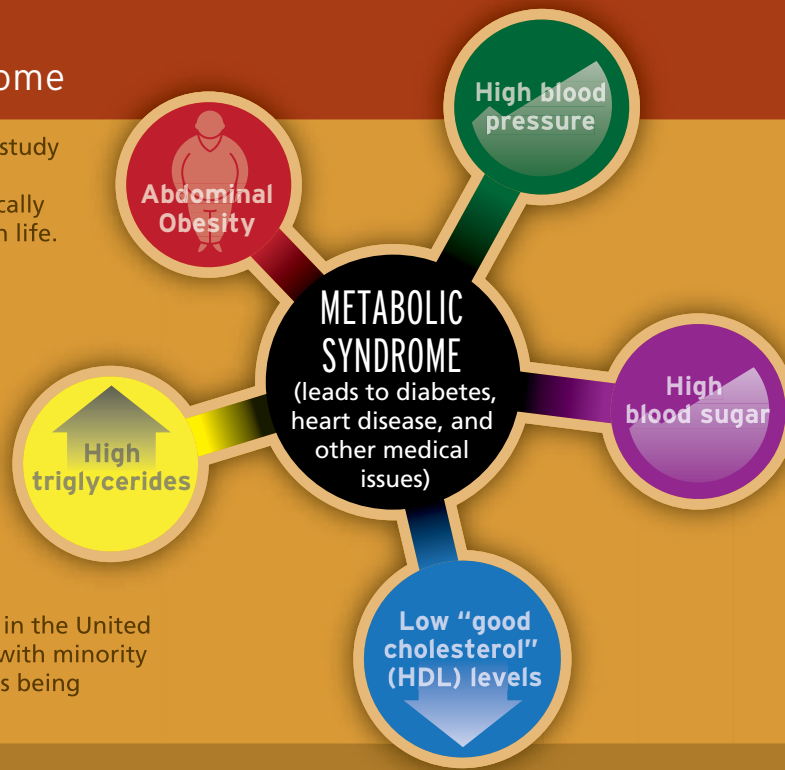
WHAT IS METABOLIC SYNDROME?

Metabolic syndrome is a cluster of early warning signs for diabetes, heart disease and other major medical problems. These warning signs, or cardiometabolic risk factors, include:

- abdominal (central) obesity,
- elevated blood pressure,
- elevated fasting plasma glucose,
- high serum triglycerides, and
- low high-density cholesterol (HDL) levels.

2.5
MILLION

Estimated number of adolescents in the United States with metabolic syndrome, with minority groups such as Mexican Americans being particularly vulnerable.

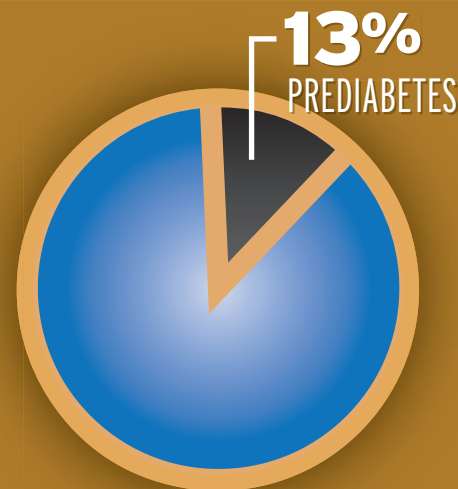
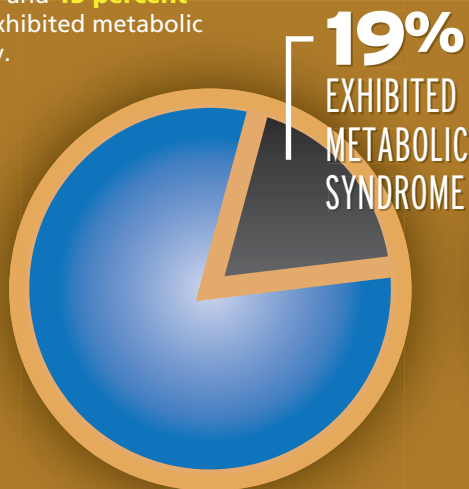
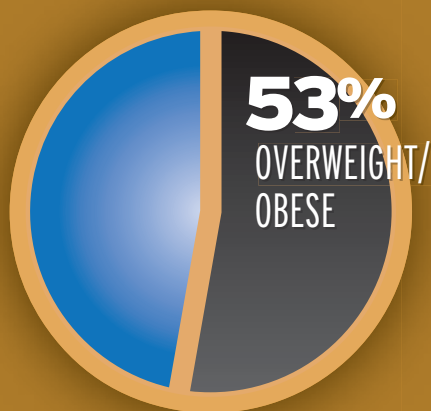


THE TEXAS BIOMED STUDY

This new study examined 670 non-diabetic boys and girls, from predominantly lower-income extended Mexican American families, many of whose adult members have increased risk of diabetes. They were enrolled in the San Antonio Family Assessment of Metabolic Risk Indicators in Youth (SAFARI) study.

THE FINDINGS

Nearly **53 percent** of the children between the ages of 6 and 17 years were overweight or obese, and **13 percent** had prediabetes. Overall, **19 percent** exhibited metabolic syndrome — **1 in 5** children in the study.



“SAFARI data suggest that if risk-factor screening of high-risk children could be performed by age 6, it could provide an opportunity for interventions that might delay or prevent their developing debilitating health conditions later in life,” said lead author Sharon Fowler, M.P.H., of the Health Science Center.

“For parents and primary care physicians, it’s a good motivating factor to intervene early if you discover that your child is at greater-than-average risk of developing diabetes or cardiovascular disease at an early age,” said Daniel Hale, M.D., chief of the Division of Pediatric Endocrinology and Diabetes in the Department of Pediatrics at the Health Science Center and medical director of the SAFARI study.

Duggirala and other SAFARI investigators are currently conducting further genetic testing to determine which specific genes directly influence disease-related risk factors in these children. Because the SAFARI data warrant immediate efforts for interventions to prevent the development of future serious health problems in these young people, the investigators have submitted an application to NIH for potential funding to conduct a 12-week-long community-based, family-centered lifestyle intervention study involving SAFARI participants. ■

Understanding How Genetic Sequence Changes Cause Disease

Genetic studies conducted by scientists around the world

AND AT TEXAS BIOMED CONTINUE TO IDENTIFY LARGE NUMBERS OF VARIANTS IN THE HUMAN GENOME THAT CONTRIBUTE TO A WIDE RANGE OF DISEASES.



☒ WE ARE *discovering differences in our DNA sequence almost daily,*

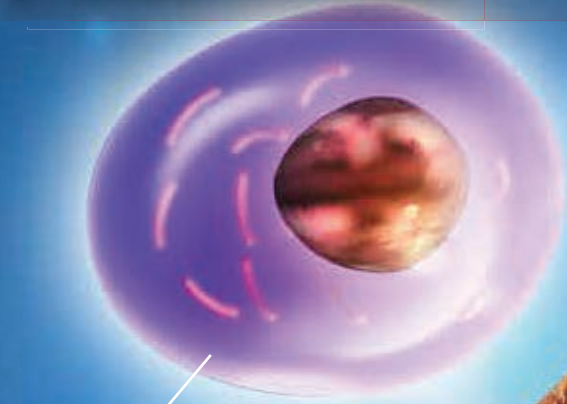
THANKS TO RECENT ADVANCES IN SEQUENCING TECHNOLOGIES.☒

— MICHAEL OLIVIER, PH.D.

Now, with the entire DNA of more and more individuals completely sequenced, the next big task in genetics will be to try and understand how all these changes in the DNA sequence affect the cells in the body and lead to obesity, diabetes, heart disease, or even neurological disorders such as Parkinson's disease. Gene sequencing allows researchers to read and decipher the genetic information found in DNA and identify variations that can result in disease.

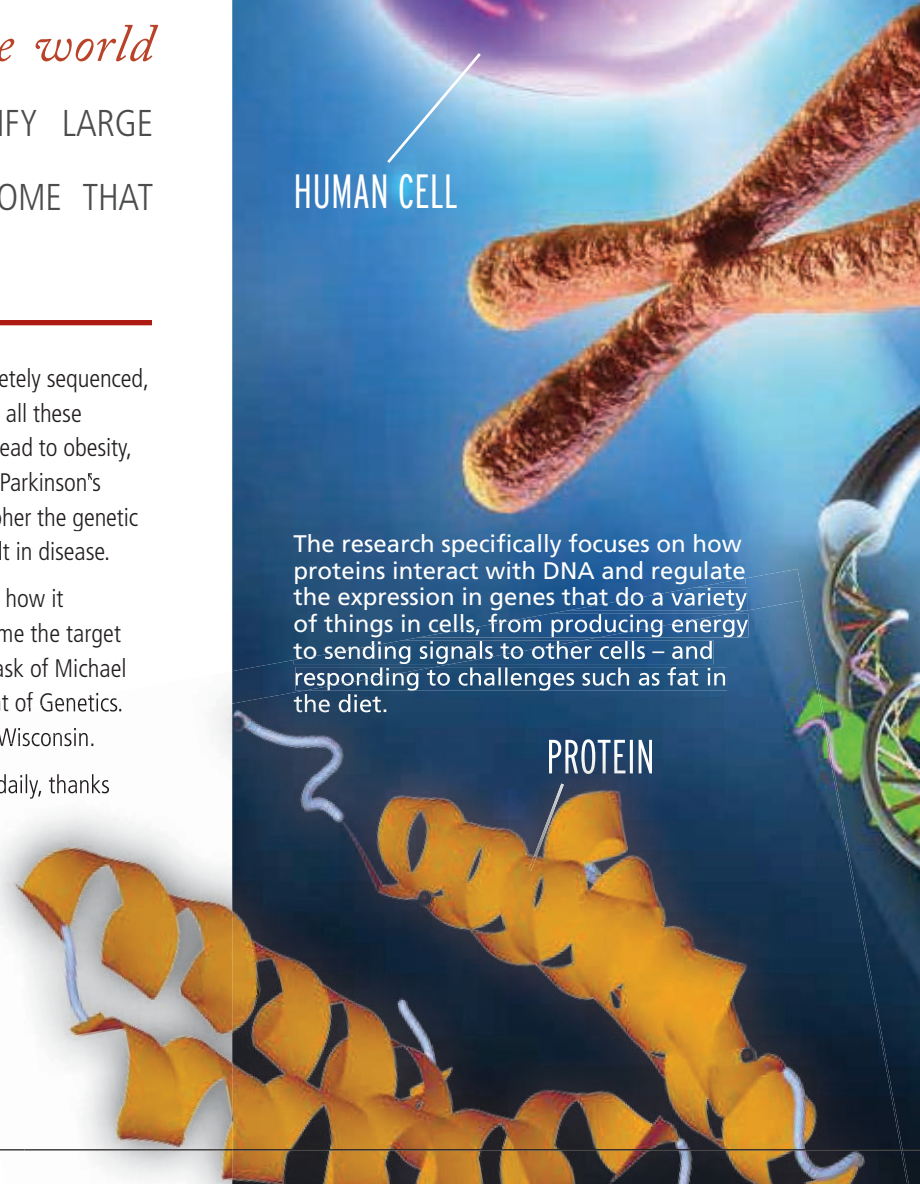
Once this genetic variation is identified and scientists discover how it changes proteins that cause disease, these proteins may become the target for therapies and help improve treatment. This is exactly the task of Michael Olivier, Ph.D., Texas Biomed's newest recruit to the Department of Genetics. He came to Texas Biomed in July from the Medical College of Wisconsin.

“We are discovering differences in our DNA sequence almost daily, thanks to recent advances in sequencing technologies,” Olivier said, “but we actually have no idea how these sequence changes modify our cells and what no longer works normally. Unfortunately, there are no technologies yet available to give us the answer to these questions.”



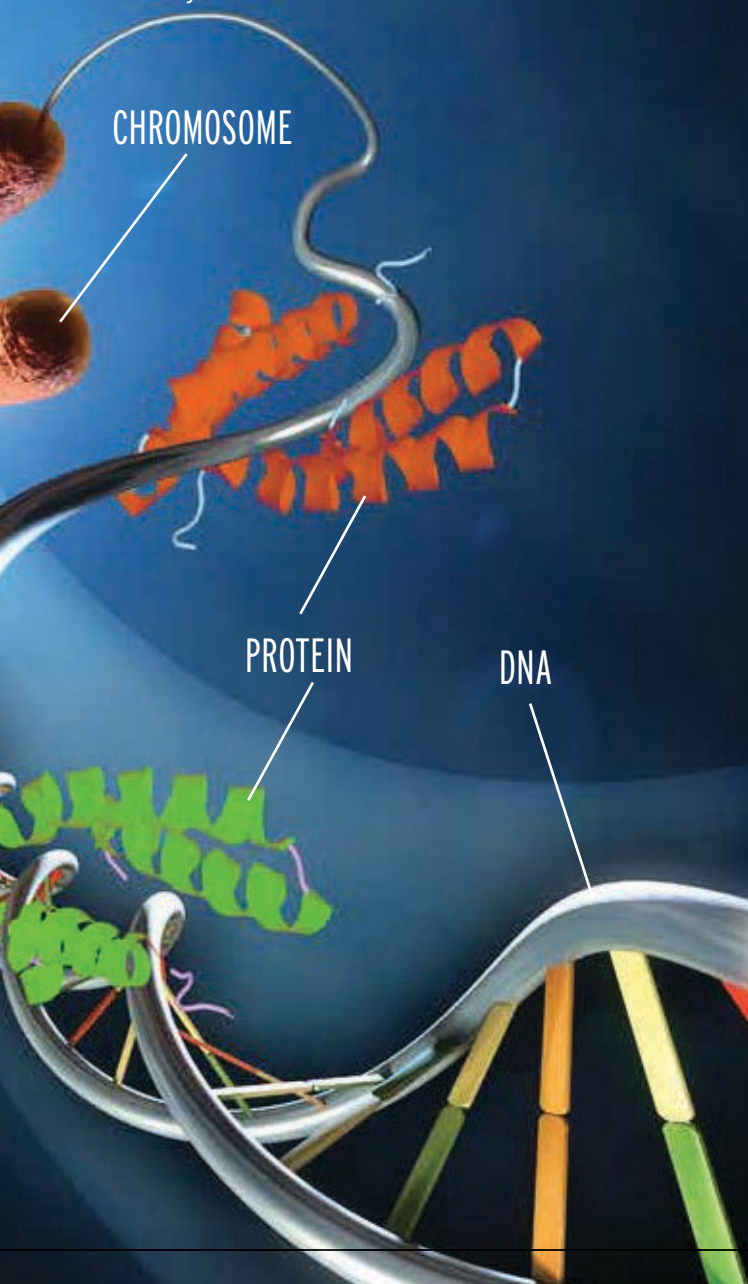
HUMAN CELL

The research specifically focuses on how proteins interact with DNA and regulate the expression in genes that do a variety of things in cells, from producing energy to sending signals to other cells – and responding to challenges such as fat in the diet.



PROTEIN

Texas Biomed scientists are currently conducting research to identify the origin of a variety of diseases and ailments, such as obesity, diabetes and heart disease. They first start with a human cell, and finally analyze the DNA itself.



NEW TECHNOLOGIES

To overcome this hurdle, Olivier's laboratory is developing novel technologies and methods, some of which are now being tested in the San Antonio Family Study. The lab specifically focuses on developing new ways to study how proteins — little machines in cells that do everything from producing energy to sending signals to other cells to recognizing and responding to challenges such as fat in the diet — interact with the DNA in our cells to regulate the expression of genes.

Genes can be turned on or off, depending on whether a cell needs more or less of a specific protein; and this complex regulation is influenced by a large number of other proteins that bind to the DNA and regulate it. These regulatory proteins bind to specific sequences in the DNA; and if this sequence is changed in an individual, that particular protein may no longer bind as efficiently. The result is that a nearby gene is regulated differently in a person with this specific change in the DNA sequence.

“Obviously, this complex regulation of genes requires a large number of different proteins, and many of them we do not even know yet,” Olivier said. “This is why we are trying to develop a method that allows us to look at one specific piece of DNA, such as one gene, and to identify all the proteins that are bound to that particular sequence.”

IDENTIFYING PROTEINS

Once the sequence has been isolated, the bound proteins can be identified by a technology called mass spectrometry that uses advanced sensitive instrumentation to detect small amounts of proteins.

The Department of Genetics has established a new mass spectrometry laboratory, directed by Olivier, which is now being used to identify the proteins that regulate genes. Olivier's group is developing the necessary protocols to apply this method to the study of human diseases as part of the Center of Excellence in Genomics Science, a collaborative project with researchers at the University of Wisconsin-Madison and the Medical College of Wisconsin, which he directs. The center receives funding from the National Human Genome Research Institute, a part of the National Institutes of Health.

In collaboration with Joanne Curran, Ph.D., Harald Göring, Ph.D., and John Blangero, Ph.D., in the Department of Genetics, Olivier will exploit this new methodology to examine cells from members of the San Antonio Family Study. Here, the investigators will identify proteins that influence genes important in the regulation of cholesterol and other risk factors for heart disease.

Previous studies have helped identify changes in the DNA sequence of study participants that raise their cholesterol levels which, in turn, increases their risk for heart attacks or strokes. This new

study will identify how these sequence changes modify the regulation of specific genes and which proteins are important in that regulation.

“Identifying the proteins that are important for this regulation of genes will not only help us understand how these sequence changes lead to higher cholesterol levels in these participants, it will also help us to identify new drugs that may help correct these changes and help reduce the risk for a heart attack or stroke,” Olivier said.

DEVELOPING NEW METHODS

For now, however, his lab is focusing on developing the protocols and methods needed to begin these investigations — a challenging effort requiring a wide range of expertise, from chemistry to genetics to cell and molecular biology. Olivier noted that when the team started on this project and proposed this method, most people loved the idea and immediately saw the benefits but also acknowledged its difficulty and questioned whether it could be done.

Although it will require more development and testing, Olivier and his group are confident that they have worked out the methodology so that it can now be used to help understand how the human genome works and how the sequence differences in it affect disease risk. ■

Genes Are Conclusively Linked to Brain Aging and Obesity

In two firsts, Texas Biomed scientists have in separate findings linked

GENES TO BRAIN AGING AND TO OBESITY — RESULTS THAT SIGNAL GREATER UNDERSTANDING OF THE GENETIC INFLUENCES ON SOME OF THE BODY’S MOST IMPORTANT FUNCTIONS.

“A key advantage of this study is that we specifically focused on large extended families, and so we were able to disentangle genetic from nongenetic influences on the aging process,” said Glahn.

GENES AND OBESITY

IDENTIFICATION OF GENES ASSOCIATED WITH BRAIN AGING *should improve our understanding of the biological processes* THAT GOVERN NORMAL AGE-RELATED DECLINE.

— JOHN BLANGERO, PH.D.

In one study, the first in a large sample, scientists from Texas Biomed and Yale University showed conclusively that the decline in brain function in normal aging is influenced by genes. A second study from some of the same researchers found that imaging studies have identified genetic components that influence both brain anatomy and body mass, providing a crucial link between genes and obesity.

“Identification of genes associated with brain aging should improve our understanding of the biological processes that govern normal age-related decline,” said John Blangero, Ph.D., a Texas Biomed geneticist and the senior author of the first paper.

The study, funded by the National Institutes of Health (NIH), was published in the *Proceedings of the National Academy of Sciences*. David Glahn, Ph.D., an associate professor of psychiatry at the Yale University School of Medicine, was the first author.

In large pedigrees including 1,129 people ages 18 to 83, the scientists documented profound aging effects on neurocognitive ability and measures of white matter in the brain. White matter actively affects how the brain learns and functions. Genetic

material shared among biological relatives appears to predict the observed age-related changes in brain function.

Participants were drawn from large Mexican Americans families in San Antonio and enrolled in the Genetics of Brain Structure and Function Study. Brain imaging studies were conducted at the University of Texas Health Science Center at San Antonio Research Imaging Institute, directed by Peter Fox, M.D.

IMPORTANCE OF LARGE HUMAN PEDIGREES

“The use of large human pedigrees provides a powerful resource for measuring how genetic factors change with age,” Blangero said.

By applying highly sophisticated analysis, the scientists demonstrated a heritable basis for neurocognitive deterioration with age that could be attributed to genetic factors. Genes also influenced decreasing white matter integrity with age. The investigators further demonstrated that different sets of genes are responsible for these two biological aging processes.

In the second study, for the first time, imaging studies have identified genetic components that influence both brain anatomy and body mass, providing a crucial link between brain anatomy and obesity.

“Our results identify two genomic regions influencing brain anatomy and body mass index: one on chromosome 17 that contributes to the development of obesity through the regulation of food intake, and a region on chromosome 3 that appears to influence the brain’s food-related reward circuitry,” said Joanne Curran, Ph.D., a Texas Biomed geneticist and first author of the paper.

The study, funded by the NIH, was published in the journal *Human Heredity*. Yale University’s Glahn is the senior author on the paper.

OBESITY CONTRIBUTES TO CHRONIC DISEASE

Obesity is a major contributor to chronic disease and disability worldwide. In the United States alone, one-third of the adult population is obese, and more than two-thirds are overweight or obese. Among young people, the prevalence of

» Genes Linked to Brain Aging and Obesity

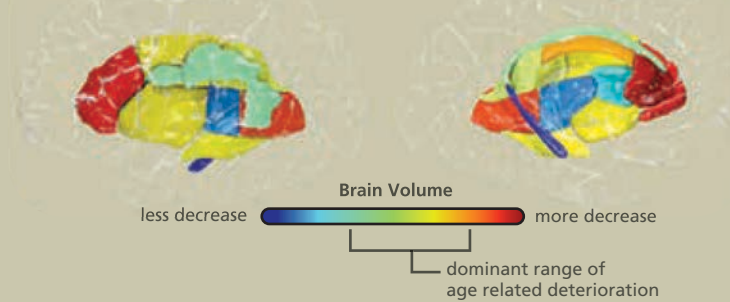
STUDY 1: LINKING GENES TO AGING

To examine the influence of the human brain on aging, scientists from Texas Biomed and Yale University studied 1,129 people aged between 18 and 83, all of whom were drawn from large Mexican American families in San Antonio enrolled in the Genetics of Brain Structure and Function Study. By applying highly sophisticated analyses, scientists demonstrated a **genetic basis to neurocognitive deterioration**.

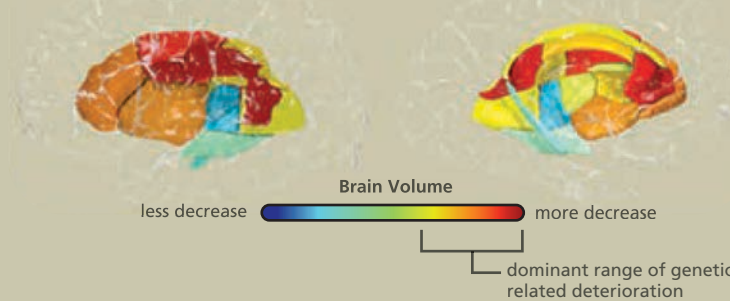
As we age, our brains decrease in volume. The images in **Group A** represent **age related change** with all areas being strongly influenced by age. The **blue color** represents a smaller **decrease in the particular brain region with age**, with a **larger decrease in brain volume** as the colors **become more red**.

Group B images represent the extent to which **genes are influencing brain volume**. The **blue color** indicates **less genetic involvement** and the **genetic involvement becomes stronger** as the **color changes to red**.

GROUP A: AGE INFLUENCED BRAIN CHANGES



GROUP B: HERITABILITY INFLUENCED BRAIN CHANGES



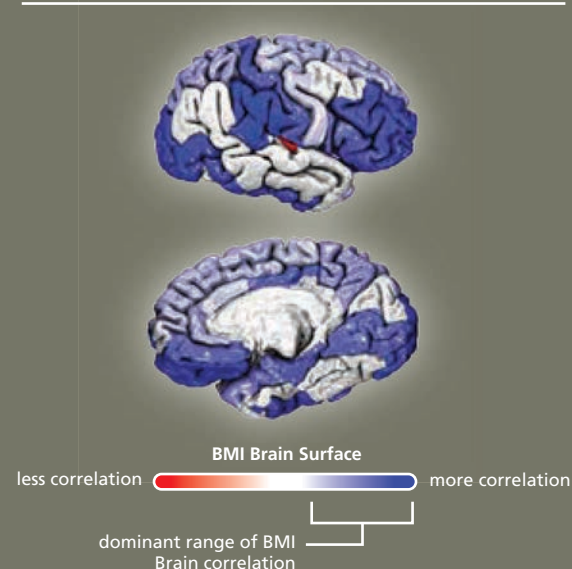
STUDY 2: LINKING GENES TO OBESITY

In another study investigating the influence of the human brain on obesity, scientists acquired MRI images of brain anatomy in 839 Mexican American individuals from large extended pedigrees. For the first time, analyses have identified genetic components that influence both brain anatomy and body mass, providing a crucial link between brain anatomy and obesity.

The images on the right represent the genetic correlations between BMI and brain surface areas. The **blue colors** represent negative correlations (the **darker the color the stronger the correlation**) indicating that the genetic factors that increase BMI act to reduce cortical surface area; the red colors represent positive correlations (the **darker the color the stronger the correlation**) indicating that the genetic factors that increase BMI act to increase cortical surface area.

Future investigation of whole-genome sequence data in these regions will identify the sequence variants influencing this brain-obesity relationship and has significant potential to lead to the identification of new obesity treatments.

CORRELATION BETWEEN BMI AND BRAIN SURFACE



obesity has tripled in the past 10 years, with 17 percent of children and adolescents now considered obese. In 2009, only two U.S. states had an obesity prevalence rate of less than 20 percent, and a staggering 33 states had prevalence rates greater than 25 percent.

The characterization of a poorly understood genetic component to disease susceptibility is very important for providing insight into this epidemic. Obesity-related traits are 40 to 70 percent heritable, yet risk genes remain elusive. The latest update of the human obesity gene map reports the identification of 127 candidate genes for common human obesity. However, only 22 of these genes are supported by multiple studies.

In the new study, MRI images of brain anatomy were acquired in 839 Mexican American individuals from large extended pedigrees. As with the first study, these studies were conducted at the Research Imaging Institute and were directed by Fox, a co-author of the paper.

The analysis showed that genetic factors associated with an increased body mass index were also associated with a reduced cortical surface area and subcortical volume. The scientists identified two genomic locations that influenced body mass index and brain areas involved in the regulation of eating behaviors.

Future use of whole-genome sequence data in these regions provides a powerful approach to finding causal variants and potential obesity treatments, Curran said. "Indeed, by discovering genes that predispose obesity risk, our eventual goal is to speed the development of drug targets to slow the epidemic advancement of obesity," she added. ■

Bob Shade, science leader at Texas Biomed for 30 years, retires

Robert E. Shade, Ph.D., arrived from Columbia, S.C.,

IN 1983 AT WHAT WAS KNOWN THEN AS THE SOUTHWEST FOUNDATION FOR BIOMEDICAL RESEARCH. LITTLE DID HE KNOW THEN THAT 30 YEARS LATER HE WOULD HOLD EVERY POSITION POSSIBLE AS A SCIENTIST AT HIS NEW INSTITUTION.

His titles at what now is Texas Biomed have included associate scientist, acting department chair in virology and immunology, scientist, acting department chair in physiology and medicine, scientific director, acting chair again in physiology and medicine and associate scientific director twice. Along the way, he also established himself as an international leader in the study of how behaviors, salt intake and hormones influence blood pressure.

Late in 2013, Shade, age 71, announced that he would retire early in 2014.

"Bob has been a gentle giant in multiple leadership roles during his 30 years at Texas Biomed," said John L. VandeBerg, Ph.D., the organization's chief scientific officer. "As a research scientist in the field of physiology, he has established a range of technologies for conducting technical procedures with nonhuman primates, and he and others have pioneered innovative research that has contributed to understanding the biological drivers of behaviors that influence healthy and disease states."

VandeBerg added that Shade excelled in his administrative roles and contributed greatly to the scientific administrative and intellectual development of the institution.

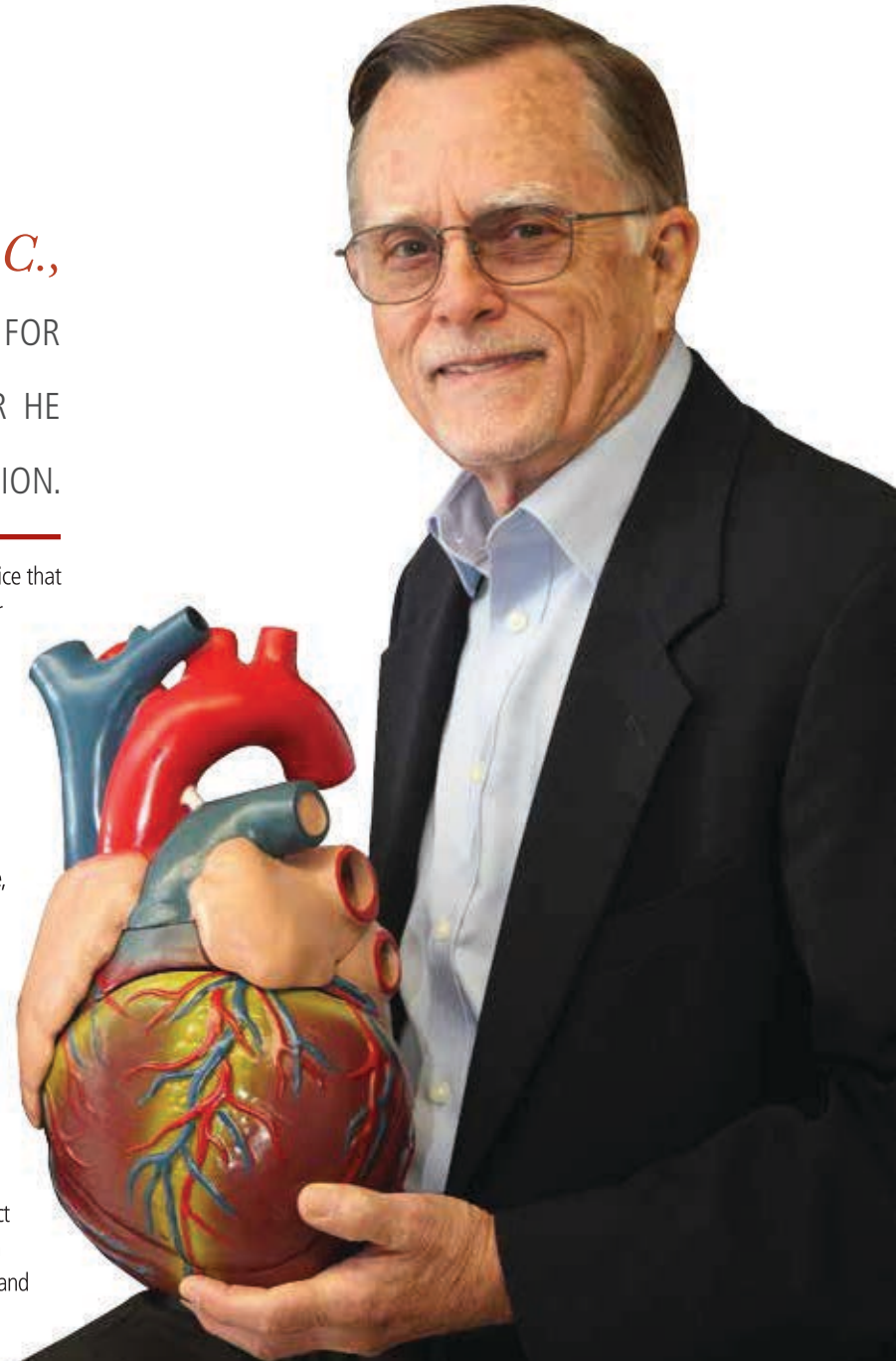
"He leaves a legacy of scientific accomplishment and service that has significantly transformed Texas Biomed into the stellar institution that it is today," VandeBerg said.

OHIO ROOTS

Growing up in the small town of Fairborn near Dayton, Ohio, Shade attended public schools and then the University of Cincinnati because of its reputation as an engineering school. By his sophomore year, his preference changed quickly through the enthusiasm of his roommate, who helped him see the excitement and promise of a career in biology.

After receiving his Ph.D. from the Indiana University Medical Center in 1970, postdoctoral study in Missouri, and teaching positions in Tennessee and South Carolina, Shade was recruited by Henry McGill, M.D., to joint positions at Texas Biomed and the University of Texas Health Science Center at San Antonio.

"I was attracted by the single investigator model and the fact that research colleagues were already in place at the Health Science Center. And Henry McGill was raising money to expand



the department of physiology and medicine,⁵ Shade recalled.

⁶"I was able to do things here that I would never have been able to do in South Carolina," he added. ⁷"I was able to interact with people in genetics and behavior, which kept me going."

He is the author of 57 published papers and two book chapters.

RESEARCH CAREER

Shade's extensive research career included many collaborations with Derek Denton, Ph.D., the founding director of the Howard Florey Institute in Melbourne, Australia. One of their studies, published in 1985 in the journal *Nature Medicine*, demonstrated unequivocally for the first time that high salt intake alone raises blood pressure in chimpanzees. The finding had important implications for human health in aging human populations because of the close similarity between the two species.

Their study showed how humans are physiologically programmed to consume salt. This had a survival value when humans were hunter-gatherers but is detrimental to survival in an environment with freely available dietary salt, the authors wrote. The study also supported the concept of screening and behavioral treatments at an early age to avoid costly expenditures on drugs later in life.

Among other findings of Shade and his colleagues are —

- Support for the concept that some forms of high blood pressure that are resistant to drugs or dietary measures might be treated by cutting the nerves that serve the kidneys, according to a study in baboons



☒ BOB LEAVES A LEGACY OF SCIENTIFIC ACCOMPLISHMENT AND SERVICE THAT HAS *significantly transformed Texas Biomed* INTO THE STELLAR INSTITUTION THAT IT IS TODAY.☒

— JOHN L. VANDEBERG, PH.D.

published in the *Journal of the American Physiological Society* in 1990. Since the study was published, scientists have found some evidence that denervating nerves is an effective way of controlling blood pressure in humans. People with hypertension typically have overactive kidney nerves, a condition that raises blood pressure and contributes to heart, kidney and blood vessel damage. In 2013, a commercial product to calm hyperactive renal nerves was under review by the Food and Drug Administration.

- That a gene located on chromosome 5 affects cell salt transport, a condition that is involved in some forms of high blood pressure. The study involved the screening of 634 pedigreed baboons at the Southwest National Primate Research Center and was published in the journal *Hypertension* in 2000. Fortunately, the salt characteristics found in baboons are identical to those found in humans. With studies such as Shade's paving the way,

Laura Cox, Ph.D., a scientist in Texas Biomed's Department of Genetics, recently received a National Institutes of Health grant to identify the genetic variants that are dysregulated by a high-salt diet. Outcomes from this study will be directly translatable to humans and provide new therapeutic targets to regulate blood pressure in individuals who are not responsive to currently available medications.

- A discovery, with colleagues from Australia, that a potent synergy among the hormones angiotensin and aldosterone stimulated salt appetite in baboons. Published in the *Journal of the American Physiological Society* in 2002, the study suggested the need for further research into this process in primates including humans. The study also provided insight into brain pathways that are activated when humans need to increase salt intake.
- Exploration of the neural correlates of the emergence of a consciousness of thirst.

Imaging studies of 10 humans by PET and MRI scans identified several brain regions that were activated by thirst and by the satiation of thirst. While recommending more study, the authors noted that gratification may turn off some brain areas that specifically subserve the consciousness of thirst and others that control neuroendocrine regulation. This study, published in 2003 in the *Proceedings of the National Academy of Sciences*, provides a potential explanation for a neural mechanism that leads to the loss of thirst with aging.

LIFE AFTER TEXAS BIOMED

So after a career in science, what's next?

Well, for one thing, Shade and his wife, Linda, will continue to restore their two-story Federal style home in San Antonio's Monticello Park district. The house was built in 1936 and purchased by them in 1983. Since then they have replaced wiring, added heating and air conditioning, a new kitchen and baths, 700 square feet upstairs, and a garage for cars and storage space. Linda retired as a senior programmer in 2013 after 27 years in Texas Biomed's Department of Genetics.

There also will be trips to Annapolis, Chicago, Seattle and San Jose to visit their four children and 11 grandchildren, all of whom are recipients of Linda Shade's handmade quilts.

⁸"The next to get them will be great-grandchildren," she noted.

For the next few years, Bob Shade will continue to conduct research at Texas Biomed — this time with an emeritus status. And both he and Linda will pursue their pastimes of cooking, gardening, yoga and restoring their home — one project that they both admit will never end. ■



With the new Earl Slick Research Center nearly

COMPLETE, THE YEAR 2013 WAS MARKED BY TEXAS BIOMED'S CONTINUING SUCCESS IN SUPPORTING AND NURTURING FIRST-RATE SCIENCE, EXPANDING ITS AREAS OF RESEARCH, AND LAYING THE GROUNDWORK FOR SIGNIFICANT PROGRESS IN THE YEARS AHEAD. HIGHLIGHTS INCLUDED RECOGNITION OF THE WORK OF INDIVIDUAL SCIENTISTS, RAISING THE INSTITUTION'S PROFILE IN TEXAS AND THE NATION, AND STRENGTHENING COLLABORATIONS WITH OTHER SAN ANTONIO RESEARCH INSTITUTIONS.

MALARIA RESEARCH IN AFRICA

Texas Biomed postdoctoral scientist Standwell Nkhoma, Ph.D., of Malawi won a prestigious \$700,000 grant from Britain's Wellcome Trust to understand the biology of malaria and improve treatment and surveillance in his native continent. Nkhoma worked at Texas Biomed from 2008 to 2013 in the Department of Genetics with Scientist Tim Anderson, Ph.D.

The grant will enable Nkhoma to conduct fieldwork in Malawi and then conduct sophisticated laboratory analyses in Liverpool and San Antonio. "We're essentially looking at how the malaria parasites interact in a human host," Nkhoma said. "In Africa, most malaria patients have multiple genotypes of parasites in one infection, which really complicates analysis of these infections."

☒ STANDWELL IS TAKING *the expertise he gained at Texas Biomed* BACK TO HIS HOME COUNTRY TO BUILD SCIENTIFIC INFRASTRUCTURE THERE AND WILL CONTINUE EXPANDING TEXAS BIOMED'S NETWORK OF COLLABORATIONS.☒

— SARAH WILLIAMS-BLANGERO, PH.D.

Malaria is responsible for 40 percent of all deaths annually and is the number one disease killer in this Southeast African country, considered one of the world's least developed nations. Malawi's life expectancy is about 52 years, compared with almost 79 years in the United States.

"Standwell is taking the expertise he gained at Texas Biomed back to his home country to build scientific infrastructure there and will continue expanding Texas Biomed's network of collaborations," said Sarah Williams-Blangero, Ph.D., Texas Biomed's Genetics Department chair.

PARKINSON'S DISEASE RESEARCH

The Perry & Ruby Stevens Charitable Foundation awarded \$1.5 million over three years to Texas Biomed to advance existing neurological research in the study of the causes of, and therapeutic approaches to, Parkinson's disease (PD).

Directed by John Blangero, Ph.D., the research will incorporate members of the San Antonio Family Study population, which is well characterized and has participants' whole genome sequence data.

PD, which afflicts as many as 1 million Americans, is a movement disorder associated with the degeneration of cells in a brain area called the substantia nigra. Unfortunately, the mechanism underlying this neurodegeneration remains poorly understood. Basically, neurons lose their ability to respond to dopamine, a critical



Award:

Malaria researcher **Tim Anderson** won designation as a Health Care Hero by the *San Antonio Business Journal*. The annual award honors leaders in the city's health care and biomedical fields.

neurotransmitter. At least 30 to 40 percent of the variability in risk of PD is the result of genetic factors.

HEALTH CARE HERO

Malaria researcher Tim Anderson won designation as a Health Care Hero by the *San Antonio Business Journal*. The annual award honors leaders in the city's health care and biomedical fields.

Anderson and his collaborators recently documented the emergence of resistance to the commonly used antimalaria drug artemisinin in western Thailand, which is a critical problem 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 effective molecular markers will be found soon with which to monitor the spread of resistance.

Williams-Blangero noted, "Tim's novel research program is highly productive and is yielding new insights into why malaria, one of the

world's major public-health problems, is so difficult to control. He brings to the battle of understanding the changing efficacy of malarial drug treatments the power of a strong research team here in San Antonio and an outstanding network of collaborators from countries in which malaria has a devastating impact."

OUTREACH TO SAN ANTONIO AND BEYOND

During 2013, Texas Biomed President and CEO Kenneth P. Trevett strengthened collaborations with other research organizations and enhanced the organization's visibility within the community. He serves on the board of the Texas Research & Technology Foundation and on the advisory boards of the Southwest Research Institute and 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 and played a significant role at its 2013 annual meeting. Gregory M.L. Patterson, Ph.D., Texas Biomed's vice president for research operations, serves as AIRI president. He previously served as secretary of its board of directors and as 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 a member of the Scientists' Center for Animal Welfare (SCAW). Anthony Comuzzie, Ph.D., a Texas Biomed geneticist, serves on the SCWA board of trustees.

Texas Biomed representatives on two occasions in 2013 visited the Washington 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.

In August, Texas Biomed's John VandeBerg, Ph.D., authored a *New York Times* op-ed piece explaining how biomedical research on captive chimpanzees is essential for developing and testing vaccines that can help save not only the lives of humans but also the lives of wild chimpanzees and gorillas.

Nonhuman primates in biomedical research was also a topic discussed in a meeting with Congressman Lamar Smith and Trevett, VandeBerg, and Jean Patterson, Ph.D., chair of the Department of Virology and Immunology. Other topics included technology transfer and Texas Biomed's new scientist recruitment and building initiatives.

During 2013, Texas Biomed opened its doors to 20 classes of high school seniors totaling more than 300 students when the Texas

Biomedical Forum hosted its annual tours for advanced biology and chemistry students. The program on exciting careers in science included a video overview of Texas Biomed and a visit to the biosafety level 4 maximum containment laboratory suit room, the AT&T Genomics Computer Center and the Southwest National Primate Research Center (SNPRC). The students heard presentations from Texas Biomed scientists working on hepatitis C, heart disease, diabetes, obesity, and other health problems. This is part of an effort of the Forum and Texas Biomed to stimulate interest among high school students in science, technology, engineering, and math careers.

Texas Biomed hosted a day-long program on the campus in June for 50 Bexar County–area science teachers. The program, which focused on class preparation, included posters, curricular materials, and a classroom laboratory demonstration kit. The program was sponsored by Silver Eagle Distributing, Inc. Jerilyn Pecotte, Ph.D., organized the day's events. Participants were greeted with a welcome from Texas Biomed President Trevett and a briefing by Vice President for Institutional Advancement Corbett Christie. Tours of research laboratories, the DNA sequencing center, the SNPRC, and the AT&T Genomics Computing Center gave the teachers an up-close view of today's biomedical research.

BUSINESS DEVELOPMENT

In April, Texas Biomed participated in the annual conference of the Biotechnology Industry Organization, where 15 meetings were held with representatives of pharmaceutical and biotech companies looking for research collaborations or



Events

In 2013, Texas Biomed either attended or hosted several events and programs:

- On two occasions in 2013 Texas Biomed visited Washington to educate elected officials and their staffs about the continuing need for the use of nonhuman primates in biomedical research.
- Texas Biomed opened its doors to 20 classes of high school seniors totaling more than 300 students hosting annual tours for advanced biology and chemistry students interested in careers in science.
- Texas Biomed hosted a day-long program on campus for area science teachers that included tours of research laboratories, the DNA sequencing center, the SNPRC, and the AT&T Genomics Computing Center.
- Texas Biomed participated in the annual conference of the Biotechnology Industry Organization, where 15 meetings were held with representatives of pharmaceutical and biotech companies looking for research collaborations or licensing opportunities.
- Texas Biomed attended the second annual vaccine symposium sponsored by the San Antonio Vaccine Development Center.

licensing opportunities. The first of a series of visits from these contacts occurred in November, and additional visits were planned for early 2014.

New opportunities for the SNPRC were pursued at two national toxicology meetings in San Antonio where Texas Biomed sponsored a booth and distributed a new booklet explaining SNPRC resources and capabilities.

VACCINE SYMPOSIUM

The second annual vaccine symposium sponsored by the San Antonio Vaccine Development Center was held in the fall and included presentations by scientists from the group's four member institutions: Texas Biomed, the University of Texas Health Science Center at San Antonio, the University of Texas at San Antonio, and Southwest Research Institute. Texas Biomed President and CEO Trevett played

a critical role in the establishment of the Vaccine Development Center in 2011.

Keynote speakers were Scott Hultgren, Ph.D., Professor and Director of the Center for Women's Infectious Diseases Research at Washington University School of Medicine, and Rafi Ahmed, Ph.D., Director of the Emory Vaccine Center at Emory University. The symposium included 14 speakers and 45 poster presentations.

TRANSITIONS

In 2013, Robert Shade, Ph.D., associate scientific director, who has worked at Texas Biomed for 30 years, announced that he would retire early in 2014. (See article, page 28.)

In addition, Jeannie Frazier, Texas Biomed's vice president for finance and administration and chief financial officer, announced that she would retire in early 2014.

"I thank Jeannie for her commitment to the organization and its mission, her personal integrity, and her "can-do" approach to problem-solving," said Trevett.

He noted that during her seven-year tenure, Frazier had a series of "clean" institutional audits, implemented important cost-saving measures, developed a very thoughtful strategy on cash management, negotiated most favorable terms on a loan for the new building, and handled many transactions related to Texas Biomed's name change in 2011. ■

Jeannie Frazier

Vice President for Finance and Administration and Chief Financial Officer, Texas Biomed, will retire in early 2014.



Financial Performance in 2013

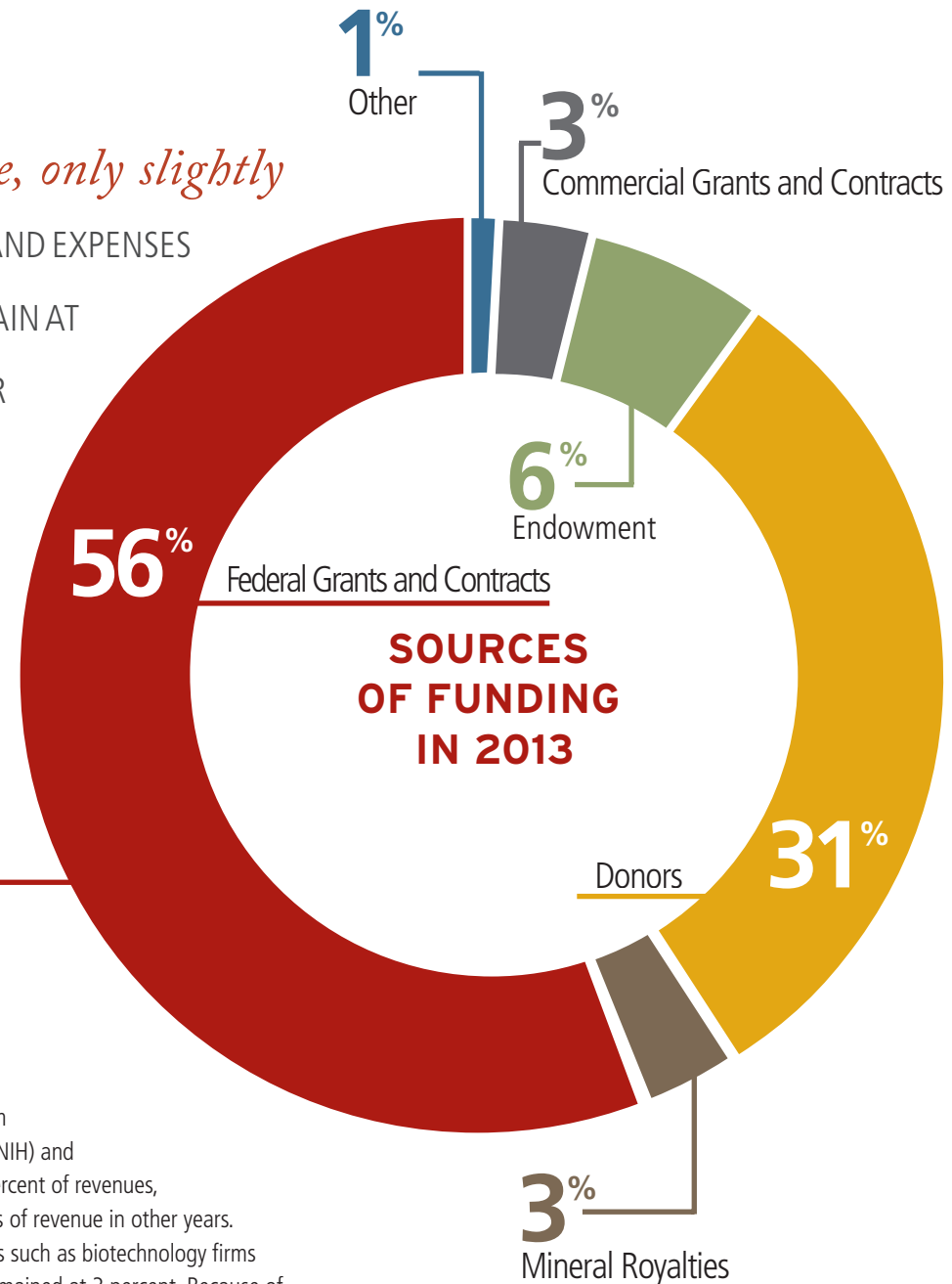
The gains from operations for 2013 were positive, only slightly

LESS THAN THE ACTUAL 2012 FIGURE OF \$1,019,000. BOTH REVENUES AND EXPENSES WERE ABOUT \$1 MILLION LESS THAN BUDGETED, WITH THE OVERALL GAIN AT BUDGETED LEVELS. JUST OVER \$17 MILLION OF THE FUNDS RAISED FOR THE NEW BUILDING WERE SPENT IN 2013. THOSE AMOUNTS APPEAR ON THE FINANCIALS AS ASSETS RELEASED FROM RESTRICTIONS. TEXAS BIOMED ALSO EXPERIENCED STRONG GROWTH IN THE ENDOWMENT, BOTH BECAUSE OF EXCELLENT INVESTMENT PERFORMANCE AND A \$4 MILLION GIFT TO THE ENDOWMENT FROM THE ESTATE OF MILTON AND GERALDINE GOLDSTEIN.

Ernst & Young's audit of Texas Biomed's operations for the fiscal year ending December 31, 2013, is expected to be completed in late spring 2014. 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 2013 will be available during the summer of 2014. Copies may be obtained through the Institute's Vice President for Finance and Administration and Chief Financial Officer Jeannie Frazier (210-258-9404).

Because donor funds for the new building were spent in 2013, and therefore recognized as unrestricted revenue, this changed the percent distribution of revenues significantly from prior years. Donations

constituted 31 percent of the funding used in 2013, up from 11 percent in the prior year. As a result, the proportion of money from other sources decreased. Peer-reviewed research grants and contracts from the National Institutes of Health (NIH) and other federal agencies were 56 percent of revenues, in contrast to about three quarters of revenue in other years. Contracts with commercial entities such as biotechnology firms and pharmaceutical companies remained at 3 percent. Because of



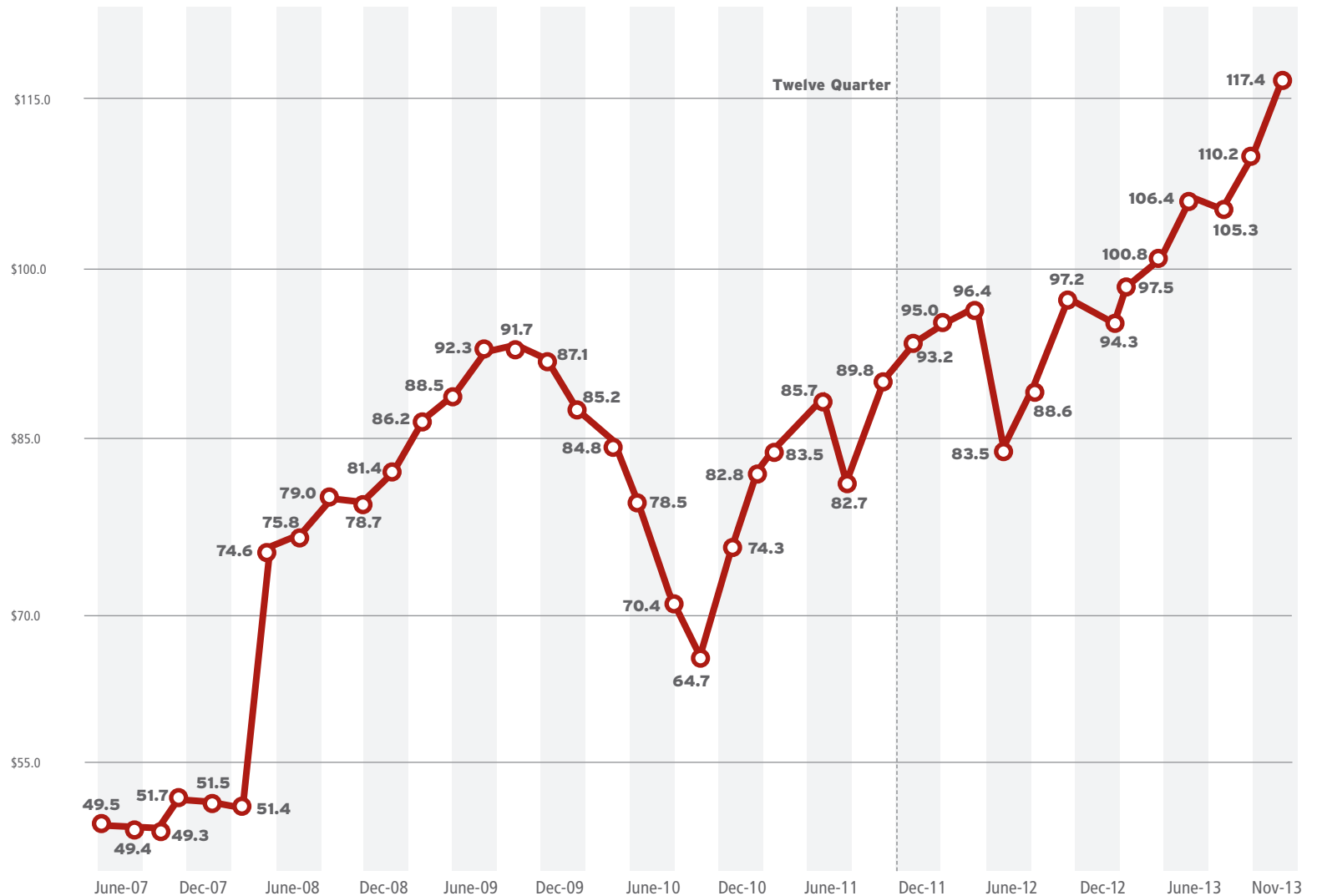
the shifting revenue proportions, this figure disguises the fact that contract revenue grew nearly 50 percent from 2012.

Donor funds totaling more than \$1.6 million from the Kronkosky, Zachry, and Voelker Foundations were used to recruit Michael Olivier, Ph.D., to the Genetics Department. The majority of this money was used to purchase a mass spectrometer. Ruth Ruprecht, M.D., Ph.D., an internationally renowned AIDS researcher, was also recruited in 2013 to the Department of Virology and Immunology.

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 2013, Texas Biomed's endowment hit its all-time high, more than \$115 million. When the investment in Evestra™ is included, the total exceeds \$117.4 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.

Texas Biomed Value of Endowment – In Millions of Dollars



This revenue, constituting 3 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 limited. ■

» 2013 NEW GRANTS AND CONTRACTS AWARDED

Federal Research Grants and Contracts

	PRINCIPAL INVESTIGATOR	LENGTH	AMOUNT TO TEXAS BIOMED
Department of Defense <i>In Vitro and In Vivo Characterization of Filoviruses</i>	Dr. Anthony Griffiths	1 Yr.	\$5,176,487
National Institutes of Health <i>CVD in American Indians Genetics Center</i>	Dr. Shelley Cole	5 Yrs.	\$2,978,289
National Institutes of Health <i>A Genetic Study of Blood Metabolites and their Relationship to Diabetes Risk</i>	Dr. Harald H. H. Göring	4 Yrs.	\$2,713,035
National Institutes of Health <i>Wisconsin Center of Excellence in Genomics Science</i>	Dr. Michael Olivier	1 Yr.	\$2,574,664
National Institutes of Health <i>Genetic Analysis of Common Diseases: An Evaluation</i>	Dr. Laura Almasy	4 Yrs.	\$2,544,520
National Institutes of Health <i>Discovery of Gene Variants and Mechanisms Underlying Salt-Sensitive Hypertension</i>	Dr. Laura A. Cox	4 Yrs.	\$1,808,040
National Institutes of Health/Bavarian Nordic A/S <i>Development of Technologies That Accelerate the Immune Response to Biodefense Vaccines</i>	Dr. Jean Patterson Dr. Ricardo Carrion, Jr.	1 Yr.	\$1,426,879
National Institutes of Health <i>Genetics of Brain Structure and Function</i>	Dr. John Blangero	2 Yrs.	\$1,093,388
National Institutes of Health/Southwest Research Institute <i>The Role of Bone Trait Covariation in Vertebral Fracture Resistance</i>	Dr. Lorena M. Havill	5 Yrs.	\$1,012,547
National Institutes of Health <i>Optimized Adaptation of Simian-tropic R5 HIV Clade C to Pig-tailed Macaques</i>	Dr. Ruth M. Ruprecht	1 Yr.	\$903,811
National Institutes of Health/Crucell <i>Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (Study 10)</i>	Dr. Ricardo Carrion, Jr. Dr. Jean L. Patterson	1 Yr.	\$602,713
National Institutes of Health <i>Vaccination against Mucosal HIV Clade C Transmission</i>	Dr. Ruth M. Ruprecht	1 Yr.	\$510,102
National Institutes of Health/Crucell <i>Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (SOW VII)</i>	Dr. Ricardo Carrion, Jr. Dr. Jean L. Patterson	1 Yr.	\$505,128
National Institutes of Health <i>Rapid Ligand Pairing Strategy to Simplify Diagnostic Immunoassay Assembly</i>	Dr. Andrew Hayhurst	2 Yrs.	\$503,250
National Institutes of Health <i>Improved Tumor Targeting of Salmonella VNP20009 Via Ice-llama Antibody Guidance</i>	Dr. Andrew Hayhurst	2 Yrs.	\$437,828
National Institutes of Health <i>Southwest National Primate Research Center Supplement</i>	Mr. Kenneth Trevett	1 Yr.	\$399,007
National Institutes of Health/Crucell <i>Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (Study 6B)</i>	Dr. Jean L. Patterson	1 Yr.	\$219,765

» 2013 NEW GRANTS AND CONTRACTS AWARDED

Federal Research Grants and Contracts

	PRINCIPAL INVESTIGATOR	LENGTH	AMOUNT TO TEXAS BIOMED
National Institutes of Health/University of North Carolina <i>Genetic Epidemiology of Causal Variants across the Life Course Phase II (CaliCo 2)</i>	Dr. Shelley Cole	4 Yrs.	\$76,004
National Institutes of Health/University of Texas Health Science Center San Antonio <i>Effects of Rapamycin on a Small, Short-Lived Primate, the Common Marmoset Supplement</i>	Dr. Kathleen M. Brasky	1 Yr.	\$73,919
National Institutes of Health <i>Infant Immunoprophylaxis against a Primate Lentivirus</i>	Dr. Ruth M. Ruprecht	6 Mos.	\$45,964
National Institutes of Health <i>Wisconsin Center of Excellence in Genomics Science Supplement</i>	Dr. Michael Olivier	1 Yr.	\$45,908
National Institutes of Health/Fisher BioServices <i>Efficacy of MVA-BN-Marv Vaccine</i>	Dr. Ricardo Carrion, Jr.	3 Mos.	\$32,867
National Institutes of Health/University of Maryland <i>SOLAR-Eclipse Computational Tools for Imaging Genetics Supplement</i>	Dr. John Blangero	1 Yr.	\$24,056
National Institutes of Health/University of Texas Health Science Center San Antonio <i>The Disablement Process in Rheumatoid Arthritis Supplement</i>	Dr. Ravindranath Duggirala	1 Yr.	\$23,215
National Institutes of Health/Johns Hopkins University <i>Arsenic Exposure, Genetic Determinants and Diabetes Risk in a Family Study Supplement</i>	Dr. Shelley Cole	1 Yr.	\$19,302
National Institutes of Health/Johns Hopkins University <i>Arsenic Exposure, Genetic Determinants and Diabetes Risk in a Family Study Supplement</i>	Dr. Shelley Cole	1 Yr.	\$19,302
National Institutes of Health/Texas Tech University <i>Filoviruses Population-Based Mapping of Schizophrenia Genes Supplement</i>	Dr. John Blangero	1 Yr.	\$11,928

TOTAL FEDERAL RESEARCH GRANTS AND CONTRACTS

\$25,781,918

Academic Research Grants and Contracts

	PRINCIPAL INVESTIGATOR	LENGTH	AMOUNT TO TEXAS BIOMED
Menzies Research Institute <i>Familial Cancer Whole-genome Sequencing and Variant Identification Supplement</i>	Dr. Joanne E. Curran	1 Yr.	\$95,690
Menzies Research Institute <i>Familial Cancer Whole-genome Sequencing and Variant Identification</i>	Dr. Joanne E. Curran	8 Mos.	\$85,000
Baker IDI Institute <i>Exome Sequencing-Mauritius Project</i>	Dr. Joanne E. Curran Dr. John Blangero	1 Yr.	\$63,655
San Antonio Vaccine Development Center <i>A Post-Exposure Vaccine for Lassa Fever</i>	Dr. Ricardo Carrion, Jr.	1 Yr.	\$50,000

» 2013 NEW GRANTS AND CONTRACTS AWARDED

Academic Research Grants and Contracts

	PRINCIPAL INVESTIGATOR	LENGTH	AMOUNT TO TEXAS BIOMED
Michigan State University <i>Acid Maltase Deficiency Gene Therapy in a Nonhuman Primate</i>	Dr. Karen Rice	1 Yr.	\$34,369
Wake Forest University <i>Bowden Exome Sequencing</i>	Dr. Joanne E. Curran	1 Yr.	\$27,270
Trinity University <i>Macrostructural and Microstructural Analysis of the Primate Corpus Callosum</i>	Dr. Karen Rice	1 Yr.	\$23,640
World Health Organization/University of Texas Health Science Center San Antonio <i>Development of Biomarkers for Praziquantel Resistance in Schistosomiasis</i>	Dr. Timothy J.C. Anderson	1 Yr.	\$15,000
University of Montreal <i>University of Montreal Single Bleed Access</i>	Dr. Robert E. Lanford	1 Yr.	\$7,052
University of Texas Health Science Center San Antonio <i>Pre-Clinical Study of a Neuroprotective Therapy for Parkinson's Disease in Nonhuman Primates Supplement</i>	Dr. Kathleen M. Brasky	5 Mos.	\$1,924

TOTAL ACADEMIC RESEARCH GRANTS AND CONTRACTS

\$403,600

Philanthropic Research Grants

	PRINCIPAL INVESTIGATOR	LENGTH	TOTAL AMOUNT TO TEXAS BIOMED
Perry and Ruby Stevens Charitable Foundation <i>Gene Discovery and Parkinson's Disease</i>	Dr. John Blangero	1 Yr.	\$1,500,000
Max & Minnie Tomerlin Voelcker Fund (Young Investigator) <i>Defining the Genetic Architecture of Macular Degeneration in Mexican American Families</i>	Dr. Matthew Johnson	3 Yrs	\$450,000
Robert J. Kleberg Jr. & Helen C. Kleberg Foundation <i>Novel Vaccine for Chagas Disease: Efficacy Testing in Baboons</i>	Dr. John L. VandeBerg	1 Yr.	\$251,373
Cowles Memorial Trust <i>The Genetic basis of Virulence in the Human Parasite Schistosoma mansoni (Cowles Fellowship)</i>	Dr. Winka Le Clec'h	2 Yrs.	\$135,926
Cowles Memorial Trust <i>Identification of Causal Pathways in CV Disease Using Whole Genome Sequence Data (Cowles Fellowship)</i>	Dr. Marcio de Almeida	1 Yr.	\$67,932
Joe and Jessie Crump Foundation <i>Advancing the Baboon Model for Liver Cancer</i>	Dr. Robert E. Lanford	2 Yrs.	\$35,000

» 2013 NEW GRANTS AND CONTRACTS AWARDED

Philanthropic Research Grants

	PRINCIPAL INVESTIGATOR	LENGTH	TOTAL AMOUNT TO TEXAS BIOMED
Texas Biomedical Forum <i>Development of a Novel Gene Pathway Analysis Method: Application to Cardiovascular Traits in the San Antonio Family Study</i>	Dr. Marcio de Almeida	1 Yr.	\$35,000
Texas Biomedical Forum <i>Mechanism and Evolution of Filoviral Monoclonal Affinity Reagent Sandwich Assay</i>	Dr. Andrew Hayhurst	1 Yr.	\$35,000
Texas Biomedical Forum <i>Identification of Translationally Active Genetic Networks in Livers of Baboons Fed a High Fat Diet</i>	Dr. Laura Almasy	1 Yr.	\$34,995
Texas Biomedical Forum <i>Generating a Model for Cystinosis in the Baboon Kidney Using Ultrasound-targeted Microbubble Destruction (UTMD) Technology</i>	Dr. Katy Freed	1 Yr.	\$34,868
Texas Biomedical Forum <i>Role of the Osteochondral Interface in Osteoarthritis Progression</i>	Dr. Lorena M. Havill	1 Yr.	\$32,478
San Antonio Area Foundation <i>Mapping Chromatin Architecture in Obese and Diabetic Adipose Cells Exposed to Common Prescriptions</i>	Dr. Jennifer Neary	1 Yr.	\$25,000
American Foundation for Chinese Medicine <i>Efficacy of Chinese Herbs on a Cell Culture Model for Triple Negative Breast Cancer</i>	Dr. Hareesh B. Nair	3 Mos.	\$9,325
Silver Eagle Charitable Fund <i>Science Teacher's Day at Texas Biomed</i>	Dr. Jera Pecotte	1 Yr.	\$3,000

TOTAL PHILANTHROPIC RESEARCH GRANTS

\$2,649,897

TOTAL FEDERAL GRANTS AND CONTRACTS

\$25,781,918

TOTAL ACADEMIC RESEARCH GRANTS AND CONTRACTS

\$403,600

TOTAL PHILANTHROPIC RESEARCH GRANTS

\$2,649,897

TOTAL COMMERCIAL RESEARCH GRANTS AND CONTRACTS

\$1,146,416

TOTAL GRANTS AND CONTRACTS AWARDED TO TEXAS BIOMED IN 2013

\$29,981,831

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 CORNER 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 US FROM RAVAGING INFECTIONS, AND EVERY AREA IN BETWEEN. THEIR PHILANTHROPY REPRESENTS ALL TYPES OF GIVING, INCLUDING SUPPORT FOR INNOVATIVE PILOT STUDIES THAT REPRESENT THE DREAMS OF OUR BRIGHTEST MINDS, RECRUITING NEW RESEARCHERS AND FUNDING OUR NEW LABORATORIES.



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 Web site at **www.TxBiomed.org** and click on **"Make a Difference."**

\$1=\$12 **PEOPLE WHO GIVE** to support innovative biomedical research do so because they see it as an investment in the future well-being of humanity. People give to Texas Biomed because they believe it's a place where they can get 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.



TEXAS BIOMED EXCELS AS A CENTER FOR SCIENTIFIC RESEARCH 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.



WHEN YOU GIVE, YOU'RE PART OF A FORWARD-LOOKING GROUP, one that is allowing scientists at Texas Biomed to take on the world's most intractable health problems. Basic research is an investment in the future. The vision of our founder, Tom Slick, was that innovative research would improve the health of generation after generation. Like Tom Slick, every donor to Texas Biomed envisions a healthier future and invests in life.

Make the difference by investing in life.

The Forum had another great year in 2013. 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, SUPPORT THE TEXAS BIOMEDICAL RESEARCH INSTITUTE.

members, give local high school science students the opportunity to tour the impressive facilities at Texas Biomed and learn about career opportunities in science.

CATHYRN LE VRIER,
PRESIDENT, TEXAS BIOMEDICAL FORUM



We kicked off the New Year with a special event on February 6 at Neiman Marcus in keeping with the upcoming gala theme, "La Gloria Havana." 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 Anthony Comuzzie, Ph.D., a scientist in the Department of Genetics at Texas Biomed. His topic, "Food for Thought: Diet and Genes in Disease Risk," gave guests insight into the studies that are conducted at the Institute. He discussed his studies regarding liquid calories and nutrition that were conducted in baboons at Texas Biomed's Southwest National Primate Research Center.

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

AS A DIRECT RESULT OF THESE FORUM SEED GRANTS, TEXAS BIOMED HAS BEEN AWARDED *more than \$25 million* IN LARGER, FEDERAL GRANTS DURING THE LAST 10 YEARS ALONE.

commitment to furthering the development of meaningful science education programs. A total of \$20,000, given jointly by the Forum and the V.H. McNutt Memorial Foundation, was granted this spring. The L.D. Ormsby Foundation also supports the science awards by funding a stipend to all applicants.

This spring also marked the conclusion of 11 student tours of Texas Biomed for the year — more than ever before. These tours, coordinated and facilitated by Forum

One of the Forum's most anticipated events, the annual gala, was held on May 4. "La Gloria Havana" transformed The Argyle. Guests were greeted with delicious food and drink with a Cuban flare, dazzling the sold-out crowd of almost 600 and raising \$200,000 in seed grants for Texas Biomed scientists. As a direct result of these Forum seed grants, Texas Biomed has been awarded more than \$25 million dollars in larger, federal grants during the last 10 years alone. A list of this year's recipients and their research can be found on page 38 of this report.

Also in May, Julie Zacher, the Forum's 43rd president, handed over the gavel. Zacher, a philanthropic force in San Antonio, in addition to being a wife and mother, was a fantastic and dedicated leader of the Forum last year. The Forum has been fortunate to have her serve as a trustee in many capacities for the

last seven years as she worked tirelessly to implement ideas and change to improve our efficiency and ensure our continued success.

The Forum returned in the fall with 11 new trustees and 23 others 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 prizes, generating a total of \$6,750 for the Forum.

September also marked the kickoff for the 2014 annual gala, which will be held on May 3, 2014, at The Argyle. The theme will be "Una Magica Notte En Toscana" and will celebrate the cuisine of this region of Italy.

Our fall lecture luncheon in November featured John Blangero, Ph.D., a scientist in Texas Biomed's Department of Genetics. His talk,

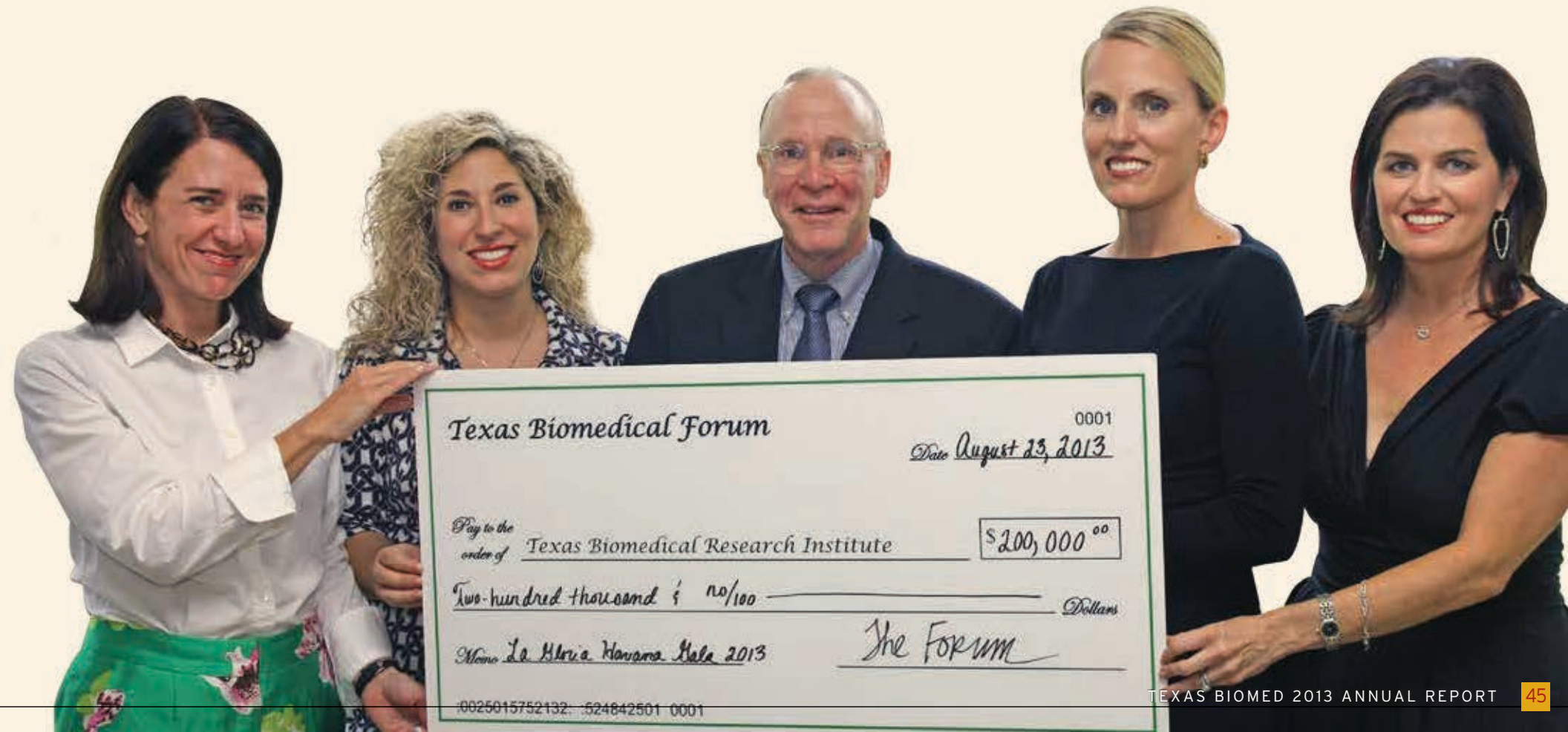
"Mining the Human Genome for the Secrets Behind Parkinson's Disease," described new studies that represent major progress in understanding what causes diseases such as Parkinson's.

In review, 2013 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 44th year, we look forward to a successful 2014 full of opportunities

to further our purpose: to support the Texas Biomedical Research Institute through community relations, volunteer service and fund raising.



CATHRYN LE VRIER
PRESIDENT, TEXAS BIOMEDICAL FORUM



Texas Biomedical Forum 0001

Date August 23, 2013

Pay to the order of Texas Biomedical Research Institute \$200,000⁰⁰

Two-hundred thousand & no/100 *Dollars*

Memo La Gloria Honors Gala 2013 The Forum

:0025015752132 :524842501 0001

The year 2013 was a record one for the Founder's Council in many



WAYS. WE CELEBRATED OUR 25TH YEAR OF HONORING THE LEGACY OF TEXAS BIOMED'S FOUNDER TOM SLICK AND OF ENCOURAGING TODAY'S YOUNG LEADERS TO BECOME COMMUNITY ADVOCATES AND FINANCIAL SUPPORTERS OF LIFESAVING GLOBAL SCIENTIFIC RESEARCH.

Tom Slick began his vision of establishing "a great center for scientific progress through biomedical research" at the age of 25, so it is only fitting that we embrace this symbolic milestone. Today, the Founder's Council membership ranges from ages 25 to 46, with the goal of building awareness among our city's young talent and creating long-term philanthropic supporters for Texas Biomed.

The Founder's Council hit another milestone in 2013 by reaching a record membership of more than 340 members. Through a variety of events, our diverse and energetic members were able to learn about the great work at Texas Biomed, meet and interact with our scientists firsthand to learn about their research, tour the campus and facilities, and simply have fun and network

with one another. In addition to our regular lecture luncheons and intimate "Dining and Discourse" event, we participated in a "Mega Mixer" with several other young philanthropic and industry groups to spread the word about the Founder's Council. Our major donors — Adventurer (\$500), Explorer (\$1,000), and Corporate (\$1,000) — enjoyed a private Hill Country picnic and bluegrass party.

Our final 25th year milestone was a record donation to Texas Biomed of nearly \$94,000 to fund competitive grants to researchers for the purchase of key pieces of scientific equipment, as well as unrestricted gifts from our higher-level members.

All in all, 2013 was a successful and exciting year and a great way to celebrate the Founder's

Council's 25th anniversary. As we start the year with our expanded campus and new buildings, we only see the enthusiasm of the Founder's Council growing, creating a pattern of long-term support that will continue to fulfill Texas Biomed's mission to improve the health of our global community for years and years to come.

Sincerely yours,

WHITNEY SOLCHER
PRESIDENT, FOUNDER'S COUNCIL

THE 2013 GRANT RECIPIENTS WERE –

- Satish Kumar, Ph.D., and John Blangero, Ph.D., for a system to measure internal function in various cell types, including stem cells.
- Laura Cox, Ph.D., for a refrigerated centrifuge to process blood samples.
- Melanie Carless, Ph.D., for a system to allow better study of genes involved in depression and mania.
- Katy Freed, Ph.D., for a device to monitor the function of a gene that goes awry in a childhood disorder — and that may help lead to new ideas for therapy.
- Matthew Johnson, Ph.D., for a biomedical freezer to preserve samples in the study of eye disorders in Mexican Americans.
- Mike Profitt, Ph.D., for a cell counter that will vastly improve efficiency in studies of cholesterol metabolism.
- Ricardo Carrion Jr., Ph.D., for an incubator to aid in tests of the effectiveness of vaccines and treatments for deadly viruses.
- Anthony Griffiths, Ph.D., for a laboratory refrigerator to store hazardous materials used in the study of viruses that jump between species.
- Andrew Hayhurst, Ph.D., for equipment to improve the study samples used in research on deadly viruses.
- Robert Baker, D.V.M., for a gas analyzer for use with anesthesia machines.
- Melissa de la Garza, D.V.M., for equipment to monitor the cardiac function of nonhuman primates.

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** Adventurer/Explorer

For more than 50 years, The Argyle, a historic Southern mansion and unique private club,

HAS BEEN DEVOTED EXCLUSIVELY TO SUPPORT OF THE LIFE-SAVING EFFORTS OF THE TEXAS BIOMEDICAL RESEARCH INSTITUTE. FOUNDED IN THE 1950s AND LOCATED ABOUT THREE AND A HALF MILES FROM DOWNTOWN SAN ANTONIO, THE 1,400-MEMBER CLUB SERVES AS A BOND BETWEEN ONE OF THE COUNTRY'S LEADING INDEPENDENT RESEARCH INSTITUTIONS AND THOSE WHO GIVE TIME AND MONEY TO SUPPORT IT.

THE ARGYLE STANDS AS
a symbol of progress
TOWARD A HEALTHIER
TOMORROW FOR THE
GLOBAL COMMUNITY

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 individuals 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, including the opportunity for questions and answers regarding the scientists' research. Argyle members enjoyed six of these chats in 2013.

Members were treated to a talk in January by Marie-Claire Gauduin, Ph.D., titled "A Novel HIV Vaccine Strategy." In February, Joanne Curran, Ph.D., spoke about "Using Genomics to Develop Better Therapeutic Drugs." In June, Michael Mahaney, Ph.D., discussed "Who Let Them in Here? Anthropologists and Genetics at Texas Biomed." In September, Michael Olivier, Ph.D., gave a presentation on "What Makes us Fat? A Tale of Genes and Proteins . . ." In October, John Blangero, Ph.D., spoke about "Mining the Human Genome for the Secrets Behind Diseases of the Brain." Finally, the year was capped off in November with Ruth Ruprecht, M.D., Ph.D., talking about "Retrovirus Research and the Route from Z to A."

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



1854

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

1884

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

1956

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

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John L. VandeBerg, Ph.D.

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Michael Olivier, Ph.D.

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BACK INSIDE COVER: Image shows Ebola virus (blue) infecting cells and causing clusters of autophagy proteins (green) to go to the cell surface that are critical for Ebola virus to infect cells. Cells are faintly grey and endosomes that the virus uses to infect cells are red.

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AND VEGETABLE-BASED INK.

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Joseph Carey, Texas Biomed Vice President for Public Affairs, Editor

Ideawire: Design & Infographics

IMAGES

Larry Walther, cover, pp. 4, 6, 8-10, 12-14, 16-19, 22, 24, 28, 30, 31, 45

Qiang Shi, M.D., Ph.D., front inside cover

File photos, pp. 7, 49

Joan Snow, p. 9

Photo courtesy of Richard Schlosberg, p. 20

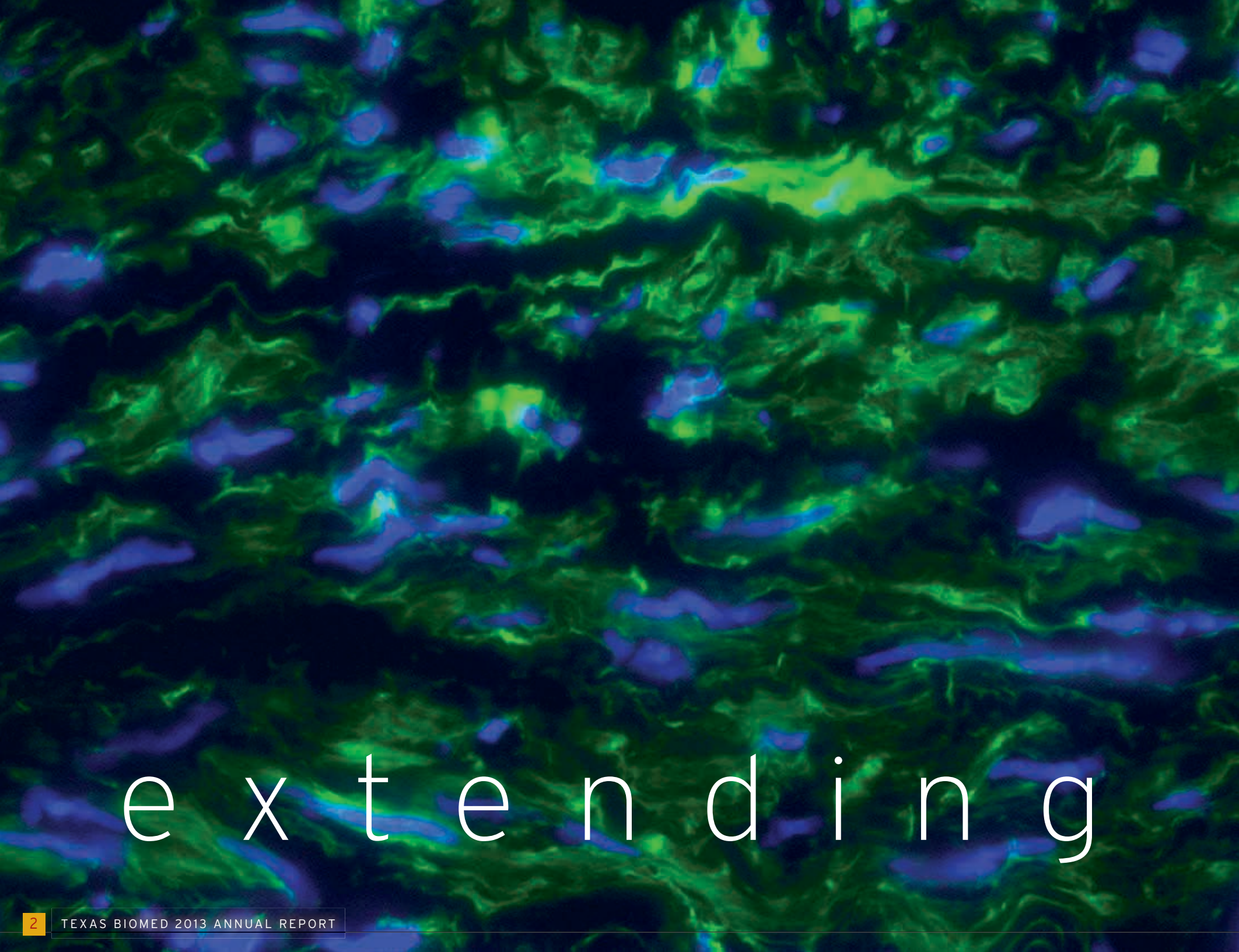
Barry Oaks, p. 29

Photo courtesy of Jeannie Frazier, p. 32

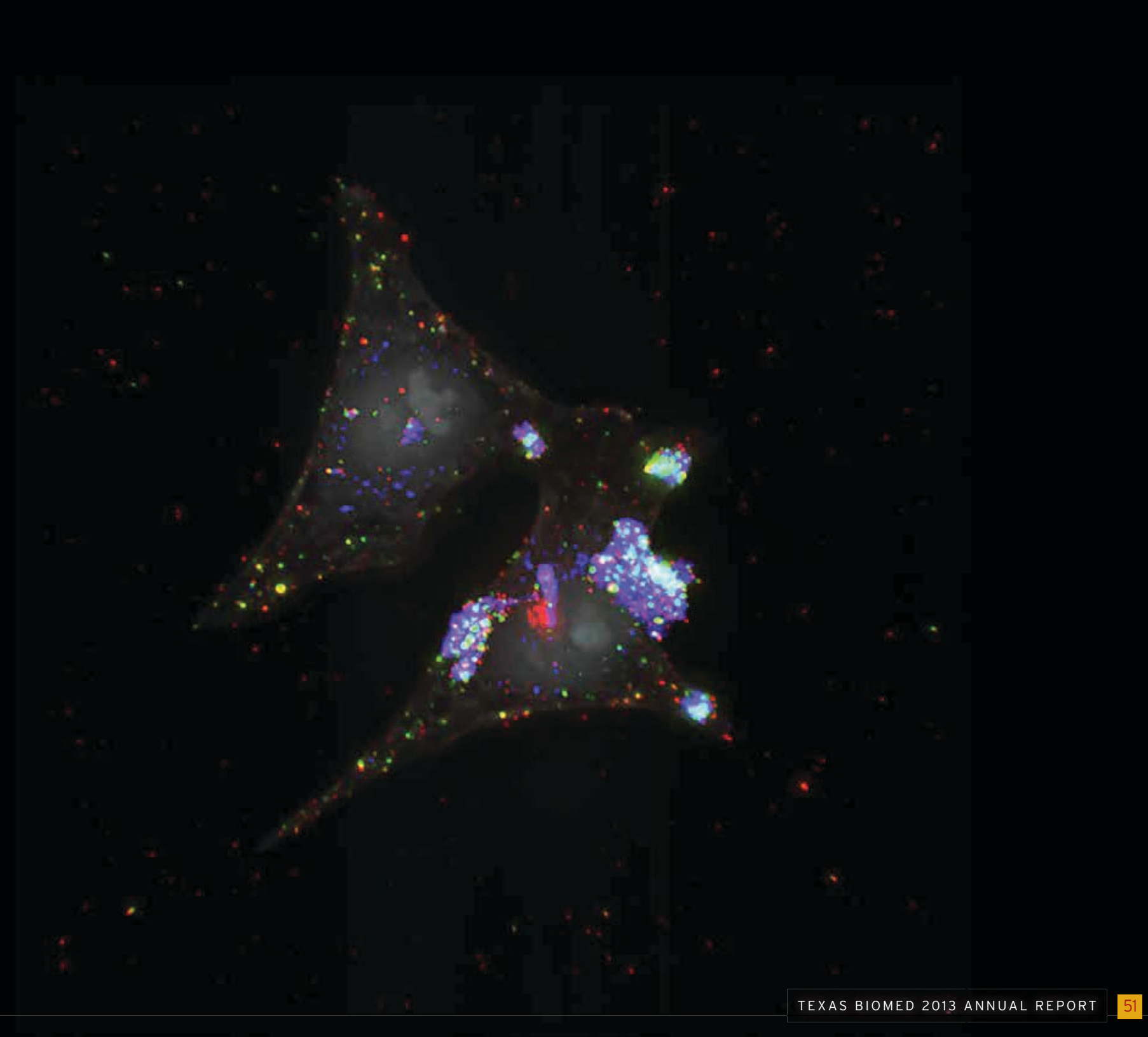
Photo courtesy of Cathryn Le Vrier, p. 44

Photo courtesy of Whitney Solcher, p. 46

Olena Shtanko, Ph.D., Davey Lab, back inside cover



e x t e n d i n g





TEXAS BIOMEDICAL[®]
RESEARCH INSTITUTE

*From the desk of
Kenneth P. Trevett,
President and CEO*

As we extend the
breadth of our
research, we thank
you for your interest in
helping us realize our
mission of improving
health worldwide.

KPT

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