The DNA of Texas Biomed

Texas Biomedical Research Institute

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Tenure began June 2016

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A letter from the president

ROBERT W. GRACY, PH.D.

In 2016 Texas Biomedical Research Institute celebrates its 75th anniversary. It is a time for us to reflect on our pioneering history and celebrate our scientific accomplishments. In preparation for our diamond jubilee, we took time in 2015 to reflect on who we are as an institution, and it is clear that our donors and scientists are the lifeblood of Texas Biomed. Together, they provide the synergy that brings us new insights, technologies and discoveries to combat the world's deadliest diseases.

Since our inception, our scientists have made great contributions to basic and clinical sciences which have led to better diagnosis, prevention and treatment of disease. For example, Texas Biomed scientists have explored genes critical to the development of cholesterol-lowering drugs, developed neonatal care technologies for premature infants and helped develop therapies to fight Hepatitis and HIV/AIDS. In 2015, Texas Biomed discoveries were profiled on the covers of the leading international scientific journals.

As we look to the future, we see hope in the fight against longtime enemies. HIV continues to infect more than 50,000 people in the U.S. each year. A priority goal of the National Institutes of Health is developing a vaccine for HIV and a cure for AIDS, and Texas Biomed scientists are leaders in this effort. Malaria, which kills more than 400,000 people annually worldwide, is a growing problem due to increased drug resistance. Our internationally recognized scientists are using new technologies to seek answers to antibiotic resistance and change the course of this and other parasitic diseases. New industry partnerships and global collaborations are ongoing in drug and vaccine development for Ebola and other emerging infectious diseases.

> We are most thankful for the community of supporters we have at Texas Biomed. Discovery and philanthropy are inherently linked at Texas Biomed and drive the research that improves lives around the world."

Connecting people who want to make a difference in the world with science that makes that difference allows Texas Biomed to study these persistent diseases and emerging threats. The Institute began with a connection between Tom Slick's pioneering and giving spirit and innovative thought leaders in science. Each study highlighted in this year's report has been supported by donors. We are most thankful for the community of supporters we have at Texas Biomed. Discovery and philanthropy are inherently linked at Texas Biomed and drive the research that improves lives around the world.

Robert W. Gracy, Ph.D.
President and CEO

our DNA: connected but unique

The structure of DNA is comprised of four bases: Adenine, Thymine, Cytosine and Guanine. Bonded together, these four bases comprise every living thing, which makes us all connected. Yet, these four bases, when structured differently, make us all unique.

Combined in different ways at different times along the chain, the four bases of Texas Biomed's DNA ensure that our goals are connected yet our science is unique.

The **A**dvancement of science, as noted in the following stories, requires a **T**alented team of professionals, **C**ommitted to learning and **G**rowing our understanding of human health and diseases.

This understanding follows years of research, which would not be possible if not for the commitment of our supporters—a team effort that connects us to a common goal of enhancing lives through discovery.

ADVANCEMENT

TALENT

COMMITMENT

GROWTH

2016 donor thank you event at Dr. Dacia and Lanham Napier's residence.

Supporters Nancy and Jeff Moorman, Trustee, and Susan and John Kerr, Trustee

Supporter Sue Marmion and Scientist Dr. Laura Cox

Trustee Richard N. Azar II and Supporters Dick and Ginger Lord and Harriett Raney

In the hunt for an end THE FIGHT AGAINST AIDS

Acquired Immunodeficiency Virus (AIDS) ranks as the third worst plague in human history. According to the United Nations Program on AIDS, about 35 million people have died from AIDS-related illnesses since the start of the epidemic. Untreated chronic infection with the human immunodeficiency virus (HIV) leads to AIDS after a number of years. Thanks to biomedical breakthroughs, AIDS is no longer a death sentence and nearly 37 million people are living longer and healthier with HIV than those who have died from the disease.

Scientists are well into the fourth decade of the fight against AIDS and the Texas Biomedical Research Institute has been on the frontlines, testing therapies in both the lab and in nonhuman primates at the Southwest National Primate Research Center. Scientists with the Institute's AIDS program are currently working on both a cure and a vaccine for HIV/AIDS.

This effort was strengthened recently by donors participating in a direct-support program, as well as donations for pilot studies from the Texas Biomedical Forum. This direct support from donors has resulted in millions of dollars in grant funding and new discoveries.

Dr. Ruth Ruprecht, Scientist and Director of Texas Biomed AIDS Research Program, aims to create what she calls a "defense-in-depth" strategy to combat HIV and develop an effective HIV vaccine.

The basic idea is to induce a person's immune defenses simultaneously at multiple levels. The first step would be to create an immune response at the mucosal barrier to trap incoming virus particles in a process called immune exclusion. The second part of the strategy is to create an immune response in the mucosal tissue and in a person's blood that can neutralize the virus and lead to the killing of infected, HIV envelope-producing target cells. The third line of defense consists of specific immune T cells that can kill infected target cells.

Thanks in large part to donor funding, this defense-in-depth strategy has shown great potential in its various stages. Dr. Ruprecht is putting the pieces together in a new $23 million program project that has been funded in 2016 by the National Institutes of Health.

A separate study from Dr. Ruprecht's team also received a $5 million grant from the NIH in 2015 to study a combination of antiviral drugs and investigative AIDS vaccines aimed at treating infants and children affected by HIV.

"Our goal is to determine whether these candidate vaccines, partnered with antiviral drugs, will not only completely suppress HIV replication in babies infected with HIV at birth, but will also induce such strong antiviral cellular immune defenses that the virus will not reemerge after all treatment is stopped," Dr. Ruprecht said.

With a similar approach aimed at creating a mucosal-targeted vaccine, Associate Scientist Dr. Marie-Claire Gauduin has been working on novel vaccine strategies using epithelial stem cells

Dr. Marie-Claire Gauduin

Dr. Ruth Ruprecht

Dr. Luis Giavedoni, Lisa Smith and 2014-2015 Texas Biomedical Forum President Melissa Morgan

as mucosal antigen-presenting cells (NIH-supported research) to advance our understanding of the role of mucosal immune responses in protection.

According to Dr. Gauduin, an ideal vaccine should provide life-long immunity against HIV infection at the site of transmission using viral antigens (or special regions or genes encoding for viral antigens that elicit an immune response) and should focus that immune response at the site of primary replication of HIV, which is the mucosa.

To fulfill these requirements, Dr. Gauduin is also proposing to develop a trans-complementary human papillomavirus (HPV)-based HIV vaccine to be tested in monkeys. This new study, which is NIH-funded, uses an alternative strategy integrating a recombinant rhesus papillomavirus (rRhPV) to induce virus-specific immune responses at mucosal genital sites to protect against both HIV and HPV transmission. This innovative strategy, if successful, has high potential to serve as a vaccine delivery system.

"The development of an effective vaccine that restricts viral replication at mucosal portals of entry remains our best hope for controlling the HIV pandemic," said Dr. Gauduin.

Thanks to a Forum grant in 2015, Vice Chair of the Department of Virology and Immunology Dr. Luis Giavedoni and his team have begun working on a project that is focused on a cure for HIV.

"Currently, HIV patients are treated with antiretroviral therapies that suppress the virus," Dr. Giavedoni explained. "However, if the drugs are stopped the virus returns."

The HIV infection process starts when a virus penetrates the cell wall of a host cell. The virus then changes its structure from a single-strand of RNA to a double-stranded DNA. The new virus DNA then integrates with the host DNA. Once the DNA is integrated, new virus is created and pushed out to infect new cells. The host now has cells not simply carrying HIV but the HIV DNA is actually a part of that person's DNA that can continue to produce virus that can infect new cells.

Using new CRISPR technology that allows scientists to cut and either remove or insert genes into a double strand DNA, Dr. Giavedoni and his team are aiming to inactivate the HIV viral DNA by causing a double break in the integrated DNA of the virus.

Lisa Smith in Dr. Giavedoni's lab has developed several CRISPR reagents against the simian immunodeficiency (SIV) virus sequence that inactivate the virus.

The Forum grant allowed the team to test the technology in vitro to develop both the concept and protocols for which they are now submitting to NIH for additional grant funding.

"Getting to Zero: End AIDS by 2030" was the World Health Organization's message for World AIDS Day in 2015. With the help of visionary supporters, Texas Biomed scientists are doing their part to reach zero.

baboon omics

DISCOVERING A NEW BIOLOGICAL SYSTEM

One aim of biomedical research is to understand basic biological processes. To advance this aim, scientists at Texas Biomed contribute significant information to the scientific community in the fight against disease and the effort to enhance human life by studying the baboon.

Thanks to the overall support of the Texas Biomed donor community and the Southwest National Primate Research Center pilot grants, scientists in the Genetics Department completed a departmental-wide project in 2015 that integrates big data and genetics in such a way that reveals new information about the liver, a critical biological system.

Because the liver plays such a key role in the development of many ailments such as metabolic and cardiovascular diseases, scientists decided to begin this "big data" project by focusing on the liver and determining a baseline for what a normal baboon liver looks like at the molecular level.

"We selected 40 young-adult, female baboons for which we already had biopsies in our tissue bank," explained Dr. Laura Cox, Scientist and Vice Chair of the Department of Genetics. "All the animals had been fed a low fat, low cholesterol diet all their lives. We picked a group uniform in age, sex and diet to determine what the normal variation would be in the liver for animals all living in the same conditions."

Scientists analyzed the samples using a four-dimensional approach, measuring abundance of RNA (genes), microRNA, proteins and metabolites. By analyzing all four of these molecules that regulate biological processes, the scientists were able to establish what a healthy liver looks like. This study was feasible because of the combined expertise and technologies at Texas Biomed.

"This was the first time such technologies have been used in nonhuman primates, which has positioned the Institute as a leading center for nonhuman primate integrated genomics research," said Dr. Michael Olivier, Scientist and Chair of the Department of Genetics. "Now that we have assembled this four-dimensional picture of the baboon liver, we can ask how much of that is normal. We can now test how much liver function can change and still be considered a healthy, normal liver."

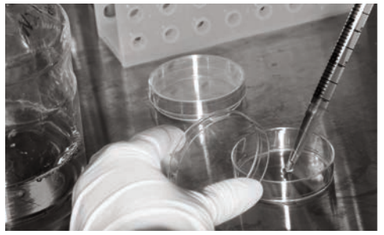
Establishing a baseline for a normal liver could not be done in humans, and having this baseline now allows scientists to study effects of many different environmental exposures on liver function, such as a high fat diet, toxins, etc., by comparing the data against this large control group.

"Regardless of the species, we now have the technology and tools in place to run these big data studies," Cox explained. "We didn't know how well this would work, but now we have the benefit of knowing we can integrate all this information and use it to tell us very useful information about important biological processes."

Dr. Biswapriya Misra, Avinash Jadhav (seated) and Dr. Jack Kent

Dr. Laura Cox, Jeremey Glenn (seated) and Ram Upadhayay

Dr. Michael Proffitt, Dr. Michael Olivier (seated) and Roy Garcia



Dr. Tiziano Barberi

stem cells

NEW RESEARCH BRINGS HOPE OF TREATMENT

The hope for a treatment that stem cell research could bring to diseases such as Duchenne Muscular Dystrophy and retinal disorders is the daily commitment of one of our scientists. Dr. Tiziano Barberi, a stem cell biologist at the Southwest National Primate Research Center, has spent the past years developing the appropriate conditions to make the right cells to begin testing the limits of what regenerative medicine can do for people suffering from these disorders.

Barberi's lab has been working with pluripotent stem cells (precursor cells to all the cells of a person's body) and differentiating them into the progenitor cells that make the retina of the eye and into skeletal muscle progenitor cells that once transplanted can hopefully replace damaged cells or delay the degeneration of cells associated with these two disorders.

"We have completed the first step in the process, which is to show that we can consistently make the cells we want with all the characteristics that lead us to believe they will function appropriately once inside a living organism," Barberi explained. "The second step is to now test in animal models whether these cells will survive, integrate and function to repair damage as they are designed."

Thanks to a grant from the William and Ella Owens Medical Research Foundation, Barberi's lab is collaborating with the Department of Ophthamology at the University of Texas Health Science Center at San Antonio to begin testing the retinal cells in a rat model of retina degeneration. In addition, a second Owens grant is supporting a collaborative study with Texas A&M University to begin a small test of the muscle progenitor cells in dystrophic dogs, which, like humans, naturally contract muscular dystrophy.

"Our hope is that we receive enough data from this small study to apply for a National Institutes of Health grant that will enable a larger study," Barberi said.

While the retinal study will need to undergo further study in nonhuman primates if shown to be effective in rats, if the stem cell therapy for muscular dystrophy shows benefit in dogs, human trials are likely to be planned as the next phase of the research.

"I specifically came to Texas Biomed and SNPRC to do translational research and move this therapy from the lab to animal models," Barberi said. "I am very grateful for the community support of these projects. It is crucial to moving these studies forward."

Dr. Barberi has also received support from the Texas Biomed Founder's Council for equipment grants, as well as the Robert J., Jr. and Helen C. Kleberg Foundation and the G.A.C. Halff Foundation as part of initial funding needed to start his lab at Texas Biomed.

Trustee Rex Amini, Dr. Ricardo Carrion, Dr. Jean Patterson and Dr. Robert Davey

fighting against ebola

SCIENTISTS LEAD THE WAY WITH COLLABORATION

The West African outbreak of Ebola virus in 2014 made Ebola a household word. The outbreak made clear that infectious diseases know no borders and have global impact, especially as we look toward yet another threat with Zika virus in 2016.

A team of scientists from Texas Biomed in the Department of Virology and Immunology, including Dr. Ricardo Carrion, Dr. Robert Davey, Dr. Luis Giavedoni, Dr. Anthony Griffiths, Dr. Andrew Hayhurst and Dr. Jean Patterson, continues their research on Ebola. The department is working with the National Institutes of Health, the Biomedical Advanced Research and Development Authority (BARDA) and the Department of Defense to develop assays and evaluate vaccine candidates.

"Texas Biomed is the only Institute of its kind in the country, with two extraordinary resources in one place—the biosafety level-4 (BSL-4) facilities and nonhuman primate colonies," said Dr. Davey, Chair of the Department of Virology and Immunology. "These resources allow for collaboration, quality control and efficiencies that no other research center can offer."

The community agreed, and in 2015, supporters gave more than $200,000 toward new Ebola research that has led to additional national funding. The direct-support program was created by several board of trustee members who have shepherded the initiative. In total, the program has raised nearly $1 million to help fund not only Ebola virus research but also HIV studies, stem cell research, a Healthy Babies initiative and in 2016 will help fund Zika virus research. Trustees spearheading this program include Richard N. Azar III, Rex Amini, John W. Feik, Abigail G. Kampmann, Bill Moll, and Richard T. Schlosberg III.

Dr. Andrew Hayhurst

This type of support is critical to scientists and helps lead to exciting discoveries like Dr. Davey's 2015 study published in *Science* magazine.

Dr. Davey and his team identified both a mechanism involved in Ebola virus infection as well as a small molecule that targets this process and holds promise as a potential therapy.

"With this research, we discovered that two pore channels (TPCs) are the key calcium sensor involved in Ebola virus infection, Davey said. "These TPCs essentially need to be turned on in order for the virus to function properly."

In the study, Davey's team determined that existing drugs currently used to treat high blood pressure have an ability to turn this key calcium sensor on and off.

He has since teamed up with scientists at the Southwest Research Institute to begin testing the small molecule, and other similar compounds, as potential therapeutics against the virus.

The National Institute of Allergy and Infectious Diseases (NIAID) also named one of Texas Biomed's scientific studies among its notable advancements in research in 2015. Dr. Manu Anantpadma, postdoctoral scientist in Dr. Davey's lab, was instrumental in a study that helped identify a critical part of the Ebola virus replication process and another potential therapeutic target.

Dr. Griffiths, Associate Scientist, and Kendra Alfson, a graduate student in his lab, also worked on a project in 2015 that led to the publication of a paper showing that Ebola virus mutates rapidly, which could serve as another target for therapeutics.

"When we started this work, there was not an appreciation that Ebola virus had any capacity to evolve and if those changes would be well tolerated," Griffiths explained.

Griffiths and his team used ultra deep sequencing to reveal that the spontaneous mutation frequency for Ebola virus was high and similar to other RNA viruses.

However, he added, "We found that Ebola virus had very limited ability to tolerate spontaneous changes in the genome, thus it was reasoned that chemically increasing the mutation frequency may decrease the number of viable virions released from a cell."

Essentially, Ebola virus has the potential to evolve rapidly but the genetic changes result in viruses that are weakened or not viable. His team is continuing their research into this process.

Before you can treat the disease, it must first be diagnosed, and Dr. Hayhurst, Associate Scientist, received a $2.3 million grant from the National Institutes of Health in 2015 to focus efforts on exploring and developing a novel mechanism of Filovirus detection using llama antibodies. This research continues his efforts begun several years ago seeking to understand the mechanism of interaction between llama antibody and virus protein. Dr. Hayhurst is collaborating with Drs. Alex Taylor and John Hart of the UT Health Science Center X-ray crystallography core lab.

Texas Biomed has been working with many different partners to test new technologies to help keep frontline healthcare professionals safer, including locally-based Xenex Disinfection Services, who tested their pulsed xenon technology against Ebola virus and anthrax spores in the BSL-4 laboratory and found it to be effective.

From helping diagnose a disease to curing them, scientists within the Department of Virology and Immunology continue the fight against pathogenic invaders and continue the search for new ways to approach global health threats.

Dr. Anthony Griffiths

Dr. Tim Anderson, 2014-2015 Founder's Council President Charley Hollimon and and Dr. Ian Cheeseman

understanding a global killer

THE RACE AGAINST MALARIA DRUG RESISTANCE

Malaria infects more than 200 million people annually, killing more than 400,000 each year, and the parasites causing malaria have developed resistance to all available classes of antimalarial drugs.

Scientist Dr. Timothy Anderson and Assistant Scientist Dr. Ian Cheeseman in the Department of Genetics are focused on understanding the emergence, mechanisms and evolution of drug resistance, which could eventually lead to more effective treatments of malaria.

Thanks to support from The Founder's Council for equipment grants over the years, both Dr. Cheeseman and Dr. Anderson have been able to develop and implement state-of-the-art technologies in the fight against malaria.

In 2015, Drs. Anderson and Cheeseman were part of a team of researchers involving the Centers for Infectious Disease Research (Seattle) and the University of Notre Dame to develop a more efficient method for creating genetic crosses between the protozoan parasites that cause malaria. This research was highlighted in the journal *Nature Methods* in July 2015.

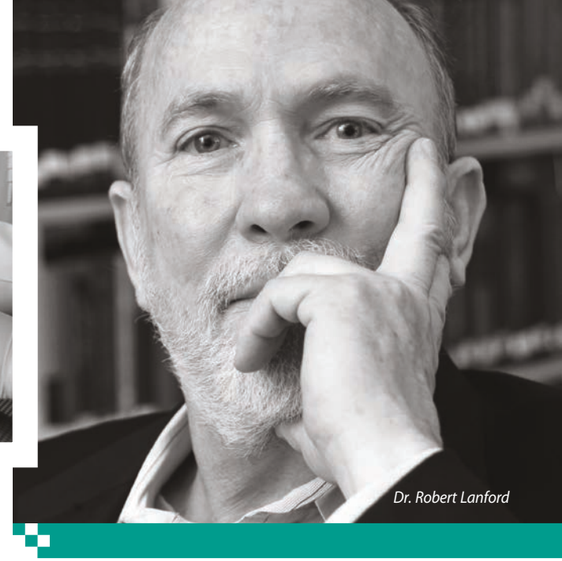
"Genetic crosses—in which we mate two parasites together and look at the characteristics of their offspring—have been an incredibly powerful tool to use with malaria parasites, but they are extremely difficult to do," explained Dr. Anderson. "The three crosses done in the past 25 years resulted in identification of parasite genes underlying resistance to multiple malaria drugs and informed multiple areas of parasite biology. This new method is cheaper and more efficient, thereby allowing us to set up bigger crosses and making our work more powerful."

Malaria infections frequently involve multiple parasites that are genetically distinct. These complex infections challenge standard genetic analysis. Dr. Cheeseman has developed a "single cell genomic" approach to isolate individual malaria parasites, amplify their genetic material and generate whole genome sequence.

This approach has allowed Dr. Cheeseman's laboratory to perform large-scale analyses of the genetic variation in malaria infections and provide genetic information on the parasites that was not available through conventional sequencing infections. This basic biological understanding of the genetics of malaria parasites can help identify potential targets for drug therapy or potential mechanisms to exploit in developing less resistant drugs.

Dr. Anderson and lab associate Shalini Nair also worked to establish the use of the CRISPR-Cas 9 technology in their laboratory. CRISPR-Cas 9 is a technology that can accurately target and modify DNA.

"Establishment of this tool in our laboratory was a major triumph, because we are now in a position to directly investigate the function of mutations that we predict will impact drug resistance and other biomedically important traits in malaria parasites," Anderson said. "These methods will be particularly important for investigating the impact of mutations on systems genetics of malaria parasites. We will be able to both demonstrate the association between candidate mutations and drug resistance, and also to investigate the biochemical pathways and metabolic rewiring that result in drug resistance."



Dr. Robert Lanford

liver cancer model

CREATING AN IMPRINT FOR THE FUTURE

Liver cancer or hepatocellular carcinoma (HCC) is the third leading cause of cancer death worldwide, and HCC has become the most rapidly increasing cause of death due to cancer in the U.S., primarily due to the hepatitis C virus (HCV) epidemic, which has infected 130 to 150 million people around the globe.

Much of our knowledge of liver cancer comes from mouse models of carcinogen exposure and/or genetically altered mice (transgenic and knockout mice). Although invaluable to our understanding of cancer, these models have limitations in the translation of potential liver cancer therapy to man. Nonhuman primates have traditionally been used as one of the models for human disease and therapy development due to their close similarity to man.

Thanks to the support of donors from around the globe, Texas Biomed started a project to develop a model of liver cancer in the baboon that will allow scientists to further explore tumor development, cancer gene function in a nonhuman primate and evaluate new potential therapeutics.

"Currently, immunotherapy is viewed as one of the most promising areas for future cancer therapy (Moon Shot Program), yet these therapies fail in most individuals for reasons that are not understood," Dr. Robert Lanford said.

Lanford's lab is taking liver cells from baboons, genetically engineering them in the lab with various cancer genes and transplanting them back into the liver of the baboons to induce liver cancer in a baboon model, which his lab has proven to be possible.

A special marker was engineered into some tumor lines to be secreted into the baboon blood, which allows detection and monitoring of tumor growth. Early tumor growth could be detected in only two weeks and tumor formation in the liver was confirmed by MRI.

"Success in growing tumors in the baboon model is a big win," Lanford said. "This new model could prove to be a highly flexible system for exploration of tumor development, evaluation of cancer gene function, and for the evaluation of new therapeutics, methods of therapeutic delivery and tumor imaging.

Already, a Texas biotechnology company is using the new baboon model to evaluate a potential therapeutic. Donor support for this project has come from The William and Ella Owens Medical Research Foundation, The Texas Biomedical Forum, Founder's Council, Joe & Jessie Crump Foundation, Max & Minnie Tomerlin Voelcker Fund, USAA Foundation, A Charitable Trust and the William Randolph Hearst Foundation.

the world of organisms

BACTERIA, HEALTH AND WELL-BEING

In recent years, scientists have learned more about the world of organisms that live inside each of us. These trillions of bacteria play important roles in a person's overall health and well-being.

While scientists have been able to calculate the approximate number of bacteria in the gut and identify various species of bacteria, little is known about how active these bacteria are and how changes in a person's activity or diet affect both the quantity and activity of the bacteria.

Thanks to a 2015 Texas Biomedical Forum grant, scientists at Texas Biomed were able to combine the resources of the Southwest National Primate Research Center with the technology of genomic sequencing and proteomics in the Department of Genetics to help identify how much and how active gut bacteria are when lifestyle factors change.

Dr. Michael Olivier, Dr. Kimberly Reeves and Dr. Prahlad Rao

Dr. Kimberly Reeves, Staff Scientist II in Genetics, has been working on identifying the types and quantity of bacteria in the gut microbiome of baboons. Her colleague Dr. Prahlad Rao, a Postdoctoral Scientist in Genetics, has developed a complementary method for analyzing proteins released by these bacteria. By measuring protein secretion, his work can help determine the activity of certain bacteria.

Dr. Reeves and Dr. Rao analyzed the number of bacteria and the proteins secreted from bacteria in baboons that were fed a healthy diet and then followed up with the same analysis in those same baboons after they were fed an unhealthy diet for seven weeks.

They are still analyzing the data, but early results show that the type and activity of bacteria are very different for the healthy and unhealthy diets. More broadly, they have demonstrated that they can measure whether a lifestyle change affects bacterial behavior. This is a first major step towards understanding how the type of bacteria in a person's gut influences overall health.

Another question scientists hope to answer is whether a person's genetic makeup influences activity of certain gut bacteria. If someone is predisposed to not having a type of bacteria that would help that person better metabolize certain foods, for example, is there a supplement that person can take to increase the amount and activity of those bacteria in their gut?

The team hopes that these initial findings will lead to human studies that include analyzing the genomes and microbiomes of specific individuals.

"Rather than comparing lots of people to one another, this allows us to analyze individuals before and after lifestyle changes to determine what influences an individual's microbiome," said Dr. Michael Olivier, Chair of the Genetics Department. "This can then help determine whether there is a lifestyle change or a probiotic or other pharmaceutical supplement that can enhance or change a person's microbiome to create the desired gut bacterial effect that would support good health."

Donors Bob Worth, Jordan Arriaga and Dr. Marcel Daadi

battling neurodegenerative diseases

WITH REGENERATIVE MEDICINE

Parkinson's disease affects more than one million Americans, according to the Parkinson's Disease Foundation. Long-time friends and supporters of Texas Biomed, Bob Worth and his family, launched a campaign last year to help Dr. Marcel Daadi, scientist with the Southwest National Primate Research Center, raise the necessary funds to begin testing a new regenerative medicine therapy for Parkinson's disease.

Raising more than $300,000 from family and friends, the funds helped launch a Good Manufacturing Practice (GMP) facility to enable Daadi to grow and begin testing the stem cell therapy in nonhuman primate models.

Still years away from possible clinical implementation, Daadi aims to grow and transplant into the brain neural stem cells that have differentiated into dopaminergic neurons, which are the cells that are lost in Parkinson's patients.

"Our family has been deeply impacted by Parkinson's disease," said Bob Worth. "We understand a cure may be years away, but Marcel's stem cell approach is just the kind of innovative, impactful science that patients and their families are looking for. Early biomedical research holds the key to a future free from Parkinson's and many other diseases."

Daadi said the funds he has received from the Worth campaign, The Perry & Ruby Stevens Charitable Foundation and other donors have allowed him to grow neural stem cells in the new GMP facility, produce and differentiate neural stem cells into dopaminergic neurons and test the MRI-guided delivery procedure of the cells into the brain of nonhuman primates. Daadi's work is also supported by the Robert J., Jr. and Helen C. Kleberg Foundation, the G.A.C. Halff Foundation and the William and Ella Owens Medical Research Foundation.

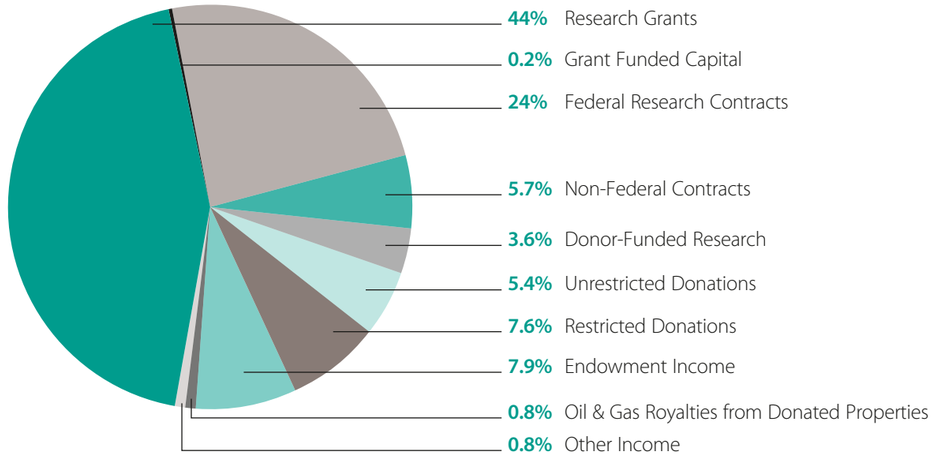
Daadi is partnering with the Department of Radiology at the University of Texas Health Science Center at San Antonio to develop a safe and effective MRI-guided delivery system of stem cells into the brain, as well as multimodal imaging approaches.

"We are making significant progress," Daadi said. "We have done our first neurosurgical transplant into a nonhuman primate, which went well. The animal recovered quickly from the procedure and was responding and playing shortly after the transplant."

This first neural transplant allowed the scientists to ensure that all processes and procedures set up were effective, and now the study is ready to move into its next phase, which is to begin testing the differentiated neural cell lines against Parkinson's in nonhuman primates.

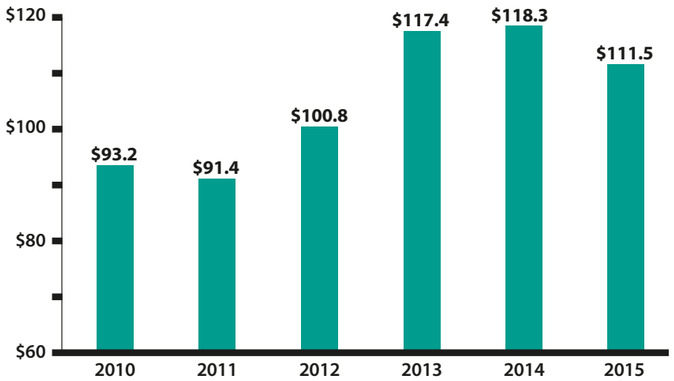
"The most exciting part of this process has been not only effectively generating these stem cell lines but also building a team and establishing all the capabilities needed to move this project forward," Daadi said. "Thanks to all the support the project continues to receive, it is just a matter of time before we have the whole package put together and results from these studies."

2015 Revenue*



* Based on 2015 Audited Financials

2015 Value of Endowment In Millions of Dollars



grants and contracts

FEDERAL (F), COMMERCIAL (C), AND MISCELLANEOUS (M) RESEARCH GRANTS AND CONTRACTS

SPONSOR	TITLE	PRINCIPAL INVESTIGATOR	LENGTH	NEW AWARD TOTAL
NIH (F)	*Establishment of a SPF Rhesus Macaque Colony*	***Dr. Robert Lanford***	*3 years*	*$8,569,989*
NIH (F)	*Functional Cure and Virus Eradication by Early HAART Plus Vaccination with Live Attenuated Rubella Virus Vectors in Macaque Infants and Neonates*	***Dr. Ruth Ruprecht***	*4 years*	*$5,021,620*
NIH (F)	*Trans-complementing Papilloma Virus for AIDS Vaccine*	***Dr. Marie Claire Gauduin***	*4 years*	*$3,397,135*
NIH (F)	*Mechanism and Evolution of Filoviral Monoclonal Affinity Reagent Sandwich Assays*	***Dr. Andrew Hayhurst***	*5 years*	*$2,360,127*
NIH/Bavarian Nordic (F)	*Immunogenicity and Protective Efficacy of MVA-BN Filo in an Ebola and a Marburg Challenge Model in Cynomolgus Monkeys (Parts 7, 8 and 9) (Jean Patterson, Co-PI) (Supplement)*	***Dr. Ricardo Carrion Jr.***	*1 year*	*$2,016,778*
BARDA/IITRI (F)	*Efficacy Studies of a Monoclonal Antibody Cocktail Against Lethal Challenges of nonhuman Primates with EBOV (CLIN 001)*	***Dr. Robert Davey***	*6 Mos*	*$1,558,931*
NIH/Bavarian Nordic (F)	*Development of Technologies that Accelerate the Immune Response to Biodefense Vaccines (Amendment 7) (Jean Patterson, Co-PI) (Supplement)*	***Dr. Ricardo Carrion Jr.***	*1 year*	*$1,545,259*
NIH/Crucell (F)	*Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (SOW 16) (Ricardo Carrion, Jr., Co-PI) (Supplement)*	***Dr. Jean Patterson***	*10 Mos*	*$978,119*
DoD (F)	*In Vitro and In Vivo Characterization of Filoviruses Through the Exploration of Various Vaccine Candidates (Clin 1,2,3,4)*	***Dr. Anthony Griffiths***	*5 Mos*	*$971,376*
NIH/Crucell (F)	*Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (SOW 18) (Ricardo Carrion, Jr., Co-PI) (Supplement)*	***Dr. Jean Patterson***	*9 Mos*	*$967,714*
NIH/Crucell (F)	*Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (SOW 13) (Ricardo Carrion, Jr., Co-PI) (Supplement)*	***Dr. Jean Patterson***	*1 year*	*$942,155*
Roche (C)	*Screening of Subsets of the Roche Library Against Ebola Virus*	***Dr. Robert Davey***	*1 year*	*$794,947*
NIH/U Colorado (F)	*A Novel Mouse Model of Obesity in Pregnancy*	***Dr. Laura Cox***	*4 years*	*$772,355*
DoD/Battelle (F)	*Novel Vaccines to Filovirus Disease in Cynomolgus Macaques*	***Dr. Anthony Griffiths***	*7 Mos*	*$733,519*
NIH/Bavarian Nordic (F)	*Development of Technologies that Accelerate the Immune Response to Biodefense Vaccines (Amendment 9) (Jean Patterson, Co-PI) (Supplement)*	***Dr. Ricardo Carrion Jr.***	*1 year*	*$653,377*
NIH/Bavarian Nordic (F)	*Development of Technologies that Accelerate the Immune Response to Biodefense Vaccines (Amendment 8) (Jean Patterson, Co-PI) (Supplement)*	***Dr. Ricardo Carrion Jr.***	*1 year*	*$653,377*
DoD (F)	*In Vitro and In Vivo Characterizations of Alphaviruses:Topic 4E*	***Dr. Anthony Griffiths***	*1 year*	*$650,048*
NIH/ UTHSCSA (F)	*Structure-guided Redesign of an Antischistosomal Drug*	***Dr. Timothy Anderson***	*5 years*	*$623,666*
NIH/UofWy (F)	*Developmental Programming by Mismatch of Pre- and Postnatal Nutrition*	***Dr. Laura Cox***	*1 year*	*$529,273*
Disruptive Tech (C)	*Quick Proof of Principle Data to Support CEP/CQ Combination IM Formulation Efficacy for EBOV*	***Dr. Robert Davey***	*1 year*	*$527,626*
NIH (F)	*Novel Broad Spectrum Inhibitors of Filovirus Infection*	***Dr. Robert Davey***	*2 years*	*$508,750*
NIH (F)	*Recombinant Papillomavirus-based HIV Vaccine Targeting Genital Mucosa*	***Dr. Marie Claire Gauduin***	*2 years*	*$508,750*
NIH (F)	*Southwest National Primate Research Center Supplement 2 (Supplement)*	***Dr. Robert Gracy***	*8 Mos*	*$440,610*
BARDA/ IITRI (F)	*Efficacy Studies of a Monoclonal Antibody Cocktail Against Lethal Challenges of Nonhuman Primates with EBOV (Guinea Pig CLIN 003 Option)*	***Dr. Robert Davey***	*8 Mos*	*$413,896*
UofWy (M)	*Mechanisms of Placental, Fetal Brain and Renal Outcomes of IUGR (Core B)*	***Dr. Laura Cox***	*1 year*	*$390,098*
NIH (F)	*The Southwest National Primate Research Center Supplement 1 (NEPRC Marmosets) (Supplement)*	***Dr. Robert Gracy***	*8 Mos*	*$318,655*
NIH/SW Res. Inst. (F)	*Targeting Therapeutics Development to Relieve Bottlenecks: Optimizing Lead Therapeutic Compounds against Infectious Pathogens*	***Dr. Robert Davey***	*1 year*	*$242,914*
DoD (F)	*Comparison of Slow and Fast Hemorrhage in Baboons*	***Dr. Karen Rice***	*1 year*	*$213,234*
NIH/Battelle (F)	*Efficacy Testing of Filovirus Vaccines in Nonhuman Primates (Ricardo Carrion, Jr., Anthony Griffiths - Co-PI) (Supplement)*	***Dr. Jean Patterson***	*8 Mos*	*$172,455*
UTHSCSA (M)	*Marmoset-Related Research Projects at the Barshop Institute*	***Dr. Suzette Tardif***	*5 years*	*$167,280*
NIH/Univ. NC Chapel Hill (F)	*Comprehensive SNP Discovery in SLC2A9. A Candidate Gene for Uric Acid Nephropathy (Supplement)*	***Dr. Shelley Cole***	*1 Mos*	*$160,672*
Arrowhead (C)	*Antiviral Efficacy of RNAi in Chronic HBV Infection Supplement #4 (Supplement)*	***Dr. Robert Lanford***	*1 year*	*$157,975*
NIH/Crucell (F)	*Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (SOW 15) (Ricardo Carrion, Jr., Co-PI) (Supplement)*	***Dr. Jean Patterson***	*9 Mos*	*$145,092*
NIH/Crucell (F)	*Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (SOW 14) (Ricardo Carrion, Jr., Co-PI) (Supplement)*	***Dr. Jean Patterson***	*1 of 1*	*$130,475*
NIH/Crucell (F)	*Advanced Development of Multivalent Filovirus (Ebola and Marburg) Hemorrhagic Fever Vaccine (SOW 19) (Ricardo Carrion, Jr., Co-PI) (Supplement)*	***Dr. Jean Patterson***	*4 Mos*	*$120,416*
NIH/Emory Univ. (F)	*Metabolic Model of Aging in the Common Marmoset*	***Dr. Suzette Tardif***	*2 years*	*$115,251*
		Total from grants under $100,000		**$1,107,012**
		TOTAL FROM FEDERAL, COMMERCIAL, AND MISCELLANEOUS RESEARCH GRANTS AND CONTRACTS		**$39,580,926**

PHILANTHROPIC RESEARCH GRANTS

SPONSOR	TITLE	PRINCIPAL INVESTIGATOR	LENGTH	NEW AWARD TOTAL
G.H.-L.Y. Mathers Fdn. (P)	*Research in Brain Function (Installment 2 of 6) (Dr. Derek Denton)*	***Dr. Laura Cox***	*3 years*	*$990,000*
Halff Foundation (P)	*Recruitment Package (Supplement)*	***Dr. Marcel Daadi***	*1 year*	*$280,760*
Various Funders (P)	*Parkinson Research-Equipment*	***Dr. Marcel Daadi***	*2 years*	*$257,042*
Halff Foundation (P)	*Recruitment Package (Supplement)*	***Dr. Tiziano Barberi***	*1 year*	*$193,840*
R.J.-Helen Kleberg Fdn. (P)	*Recruitment Package*	***Dr. Tiziano Barberi***	*1 year*	*$159,200*
		Total from gifts under $100,000		**$617,459**
		TOTAL FROM PHILANTHROPIC DONATIONS		**$2,498,301**

CONSTRUCTION AND RENOVATION GRANTS

SPONSOR	TITLE	PRINCIPAL INVESTIGATOR	LENGTH	NEW AWARD TOTAL
NIH (F)	*Renovation of Facilities for Macaque Housing at the SNPRC*	***Dr. Robert Lanford***	*1 year*	*$498,810*
Halff Foundation (P)	*Halff Research Laboratory*	***Dr. Greg Patterson***	*1 year*	*$250,000*
		TOTAL FOR CAPITAL GRANTS		**$748,810**
		GRAND TOTAL OF NEW GRANTS AND CONTRACTS AWARDED		**$42,828,037**

champions of discovery

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texas biomedical forum

"The Forum provides opportunities for its members and friends to learn directly from the scientists at Texas Biomed on issues relative to diseases being studied at the Institute."

The Texas Biomedical Forum is a non-profit group of more than 400 women from throughout San Antonio who serve as ambassadors for Texas Biomed in the community. Established in 1971, the Forum was developed specifically to support Texas Biomed through community relations, volunteer services and fundraising.

Each year the Forum invites high school students from across the city to participate in tours at Texas Biomed. More than 300 students participated in these tours in 2015. Students learned about the many exciting discoveries happening at the Institute and the opportunities to further their own learning and a possible career in science.

The Forum also provides opportunities for its members and friends to learn directly from the scientists at Texas Biomed on issues relative to diseases being studied at the Institute. These activities started with a Roundtable Discussion in January where six scientists representing the departments of Genetics, Virology & Immunology and the Southwest National Primate Research Center visited with both Forum and Golden Circle members over a light dinner. A lecture luncheon in March enlightened our members about the life of the founder of Texas Biomed, Tom Slick, through a presentation made by Mr. Slick's niece, Catherine Nixon Cooke. In November, Texas Biomed Scientist Dr. Anthony G. Comuzzie gave a lecture on "The Sweet Life: the Causes and Consequences of Diabetes".

During the spring lecture luncheon, the Forum also celebrated its Annual Science and Education Awards organized by Sara McCamish and Lynette Embrey in conjunction with the generosity and dedication of Valerie Guenther and the V.H. McNutt Memorial Foundation. Cash awards totaling $20,000 were given to area high school teachers whose innovative project proposals showed a significant commitment to science education in our community. The L.D. Ormsby Foundation also supports the science awards by funding a stipend to all applicants.

The Forum's annual gala is a premier event in San Antonio and is the foundation of the group's fundraising efforts each year. The 2015 "Fly Me to the Moon…Let me Play Among the Stars" Gala was held May 2nd, chaired by Jordan Arriaga and co-chaired by Courtney Percy. Nearly 600 guests enjoyed another sold-out evening of festivities, raising $215,000.

These funds are provided to Texas Biomed scientists as "seed" monies to initiate new pilot projects that could eventually turn into larger-scale research studies with greater funding. A list of this year's recipients and their research can be found on page 28 of this report.

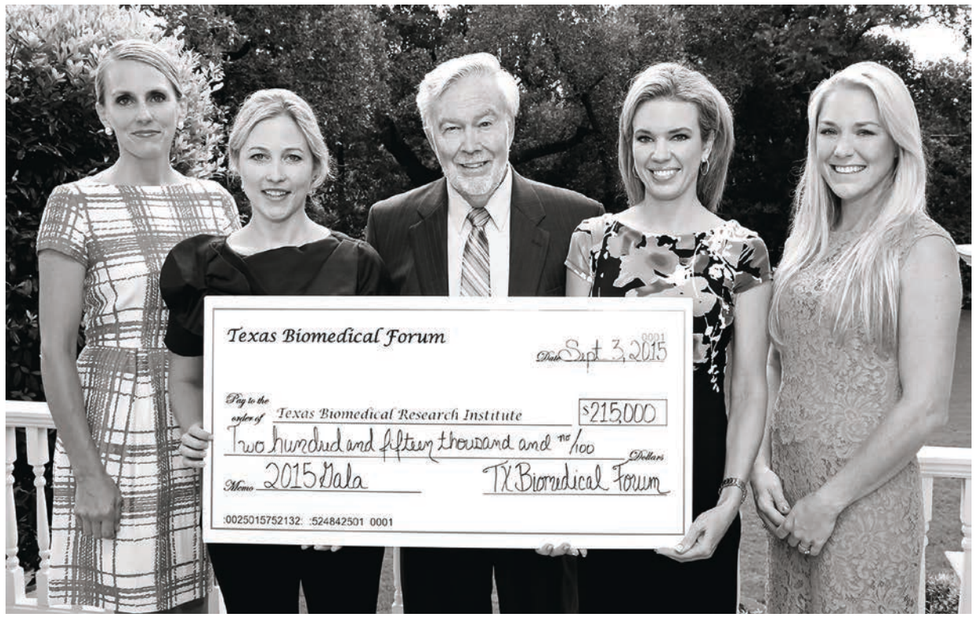
The year closed out with a November luncheon honoring past presidents of the Forum at the home of one of the past presidents, Walton Gregory. It is through the vision of the women that founded the Forum and the continued enthusiasm and dedication of our current membership and leadership that we are able to provide Texas Biomed with passionate volunteers and critical funds necessary to support research that saves lives.

Sincerely,

Amanda Bezner

Amanda Bezner
2015-2016 Forum President

▶ See Forum Grants, next page



Pictured above from l to r: Forum 2014-2015 President Melissa Morgan, 2015 Gala Co-Chair Courtney Percy, Texas Biomed President and CEO Dr. Robert Gracy, 2015 Gala Chair Jordan Arriaga, and 2015 Assistant Gala Chair Sara Walker.

The Forum awarded $215,000 *in grants to scientists at Texas Biomedical Research Institute to assist in developing preliminary data that will enable these scientists to secure future funding for novel projects. The following projects were funded in 2015.*

Tim Anderson *Genetics*	*Genetic Manipulation of Schistosome Parasites*
Luis Giavedoni *Virology & Immunology*	*Proof-of-Concept Studies Aimed at Curing HIV Infection*
Prahlad Rao and Kimberly Spradling-Reeves *Genetics*	*Systems Biology Analysis of Gut Biocrobiota in the Baboon Model of Obesity*
Marcel Daadi and Geoff Clark (UTHSCSA) *Primate Center*	*Imaging Dopaminergic Grafts in Nonhuman Primate Model of Parkinson's Disease*
Anthony Comuzzie and Michael Olivier with Nick Musi (UTHSCSA) *Genetics*	*Mechanism of Appetite Control in Lean Individuals in Families with History of Obesity*
Ruth Ruprecht and Davenport Crystal (UTHSCSA) *Virology and Immunology*	*Structural Analysis of a Monoclonal Antibody that Targets a Novel Region on HIV-1 gp41*

2015

the founders council

Founder's Council gives members the opportunity to meet and learn from the scientists."

The Founder's Council is a dynamic group of individuals between the ages of 25 and 46 with the goal of building awareness among our city's young leaders and creating long-term philanthropic supporters for Texas Biomed.

The Founder's Council was established in 1988 and now boasts more than 330 members from across San Antonio. Members' annual donations help fund competitive grants to Texas Biomed scientists, and their outreach in the community is of great value as we seek to encourage more young professionals to become advocates for scientific research.

In 2015, The Founder's Council was able to give Texas Biomed $75,000 toward the purchase of key pieces of scientific equipment. In addition, lecture luncheons are an opportunity for members and their friends to learn more about Texas Biomed's research and scientists.

The Founder's Council kicked off the year in February 2015 with a lecture luncheon featuring Scientist Dr. Marcel Daadi speaking on "Developing a Stem Cell Treatment for Parkinson's Disease." A second lecture luncheon was held in June featuring Scientist Dr. Ian Cheeseman discussing "The Threat of Emerging Malarial Drug Resistance." The final lecture luncheon was held in October featuring Scientist Dr. Robert A. Davey speaking on "Advances in Understanding Ebola virus and Finding Treatments."

In March 2015, members enjoyed the premiere event, Dining and Discourse, where scientists from across all areas of research joined a table of guests in an intimate setting over dinner, allowing for conversations about their area of expertise.

Throughout the year, we held several networking events for members and prospective members. Our Adventurer and Explorer members who support The Founder's Council at a level of $500 and above were treated to an "Epicurean Experience" at The Argyle. Members enjoyed socializing while having each course of a seated dinner paired with a wine.

At the Tobin Estate Holiday party, we were honored to present the scientists with their equipment grant awards for the year.

The Founder's Council gives members the opportunity to meet and learn from the scientists, share what they've learned in the community and then support these scientific discoveries financially. The activities and fundraising support enables our members to play a vital role in helping Texas Biomed make a global impact, and we are proud to carry on this great tradition.

Sincerely yours,

Jordan W. Arriaga

Jordan W. Arriaga
2015 President, Founder's Council

▶ *See The Founder's Council Members, next page*

2015 the founders council

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> For 60 years, this historic Southern mansion and unique private club has supported the life-saving efforts of Texas Biomedical Research Institute."

As headquarters for a horse ranch in 1854, The Argyle mansion was an outpost of Texas hospitality. In 1954, Betty Slick Moorman, sister of founder Tom Slick Jr., suggested the establishment of a high-caliber club. Members would make an annual contribution to Texas Biomed as a way to create a broader base of support for Texas Biomed; thus The Argyle of today was formed.

For 60 years, this historic Southern mansion and unique private club has supported the life-saving efforts of Texas Biomedical Research Institute. With more than 1,500 members, The Argyle 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's commitment to excellence continues today. Members welcomed many changes from personnel to facilities to member services in 2015. The Argyle kitchen was originally designed and built more than 30 years ago and was redesigned in 2015 to help increase flexibility for its staff and efficiency for members to enhance the member experience. The entire kitchen was converted to LED lights, allowing for cost savings. The new renovations have also allowed the number of meals being served to increase exponentially. The elevator and lobby have been updated to allow a more pleasurable experience for members. The Tree Room received designer chairs for all tables to match the drapes, and new paintings were displayed on the walls to commemorate the history of The Argyle. The front lawn was replaced with Celebration Bermuda grass and a Crepe Myrtle tree was planted in the Atrium, along with the addition of a new water fountain and plantings for members' enjoyment.

The Argyle is the scene for many grand occasions such as weddings and family events. Members enjoy the Sunday Jazz Brunches along with other musical entertainment. The Argyle also hosted the Worldwide Club Managers Association Convention Tour in 2015, which consisted of 1800 club managers from all over the world, receiving praise for being one of the finest clubs.

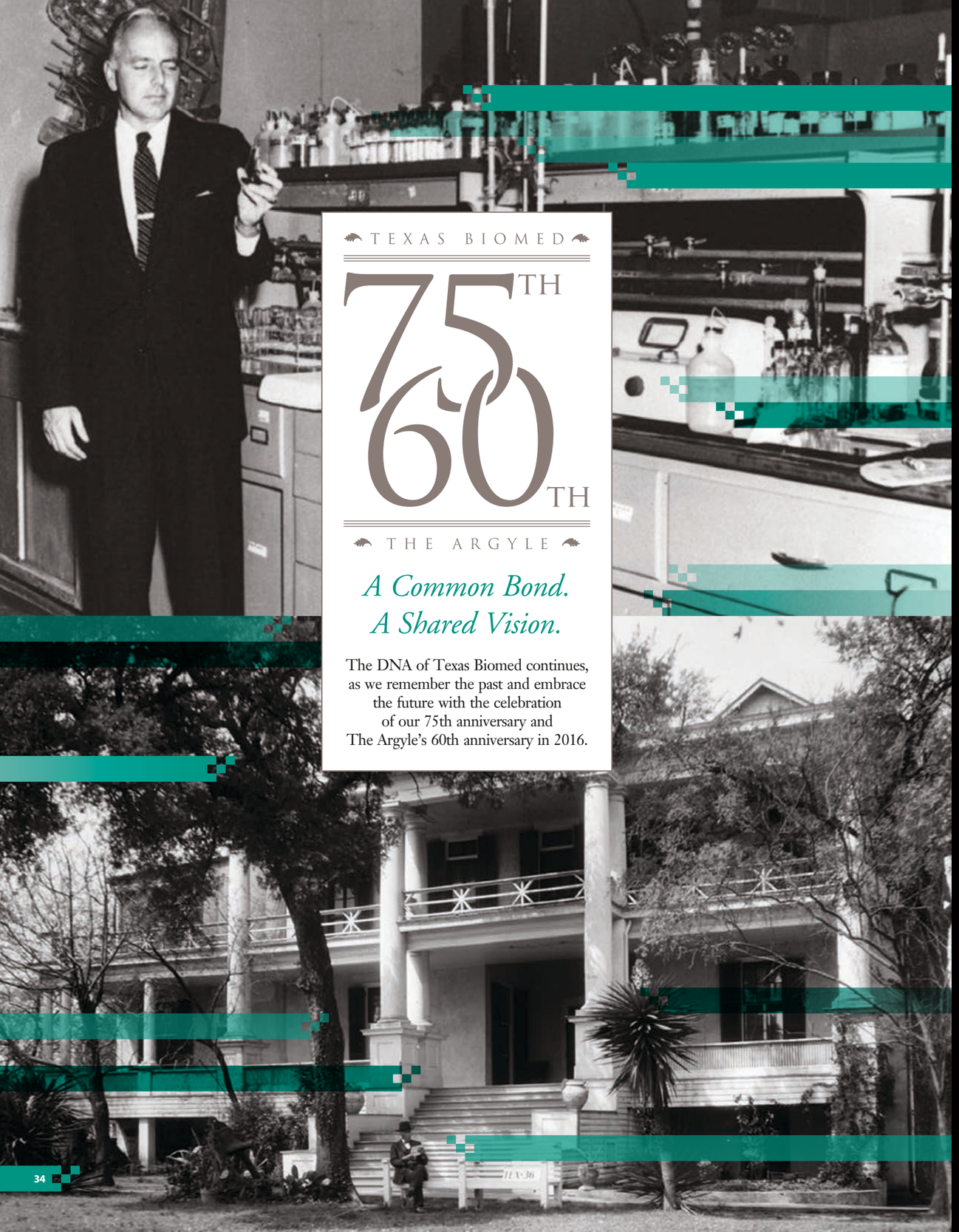
Building a bridge between science and the community, The Argyle continued one of the most popular initiatives called the "Fireside Chats." This program allows members and their guests to meet with Texas Biomed scientists in a social setting to enjoy a conversational exchange of ideas, including the opportunity for questions and answers regarding the scientists' research.

Dr. Tiziano Barberi, Scientist in the Southwest National Primate Research Center, kicked off the 2015 talks in January, discussing his work on stem cell treatment for diseases of the eye. The ability to coax stem cells to generate specialized cells/tissues for therapeutic purposes could lead to possible treatment of degenerative eye diseases.

In April, Dr. Suzette Tardif, Associate Director for the Southwest National Primate Research Center, discussed the story of Rapamycin, a compound discovered in the soil of Easter Island, that became a top 10 scientific breakthrough in 2009 when it was shown to extend the healthy lifespan of mice.

In the Fall, Associate Director of Veterinary Resources and Research Support of the Southwest National Primate Research Center, John Bernal, D.V.M., discussed the importance of animals and their veterinary care on the advancement of biological research.

The Fireside Chats continue to attract greater crowds and enthusiasm into 2016.



TEXAS BIOMED

75TH 60TH

THE ARGYLE

A Common Bond. A Shared Vision.

The DNA of Texas Biomed continues, as we remember the past and embrace the future with the celebration of our 75th anniversary and The Argyle's 60th anniversary in 2016.

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The 2015 Annual Report is a publication of the Texas Biomedical Research Institute.

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Lisa Z. Cruz,
Texas Biomed Director of Public Relations, Editor

Jeffrey Heinke Design,
Design

Claudia Olivier,
Contributing Editor

IMAGES

Greg Harrison Photography

File photos

Argyle Hotel in 1936, courtesy of the Library of Congress

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Texas Biomedical Research Institute
P.O. Box 760549, San Antonio, TX 78245
www.txbiomed.org
210.258.9400