TEXAS BIOMEDICAL RESEARCH INSTITUTE

FALL 2013

PROGRESS

Enhancing lives through discovery™

Chasing Potential Bioterror Threats

Scientists target anthrax, Ebola and Marburg viruses and more

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INSIDE:

Texas Biomed hires two world-class scientists in genetics and virology

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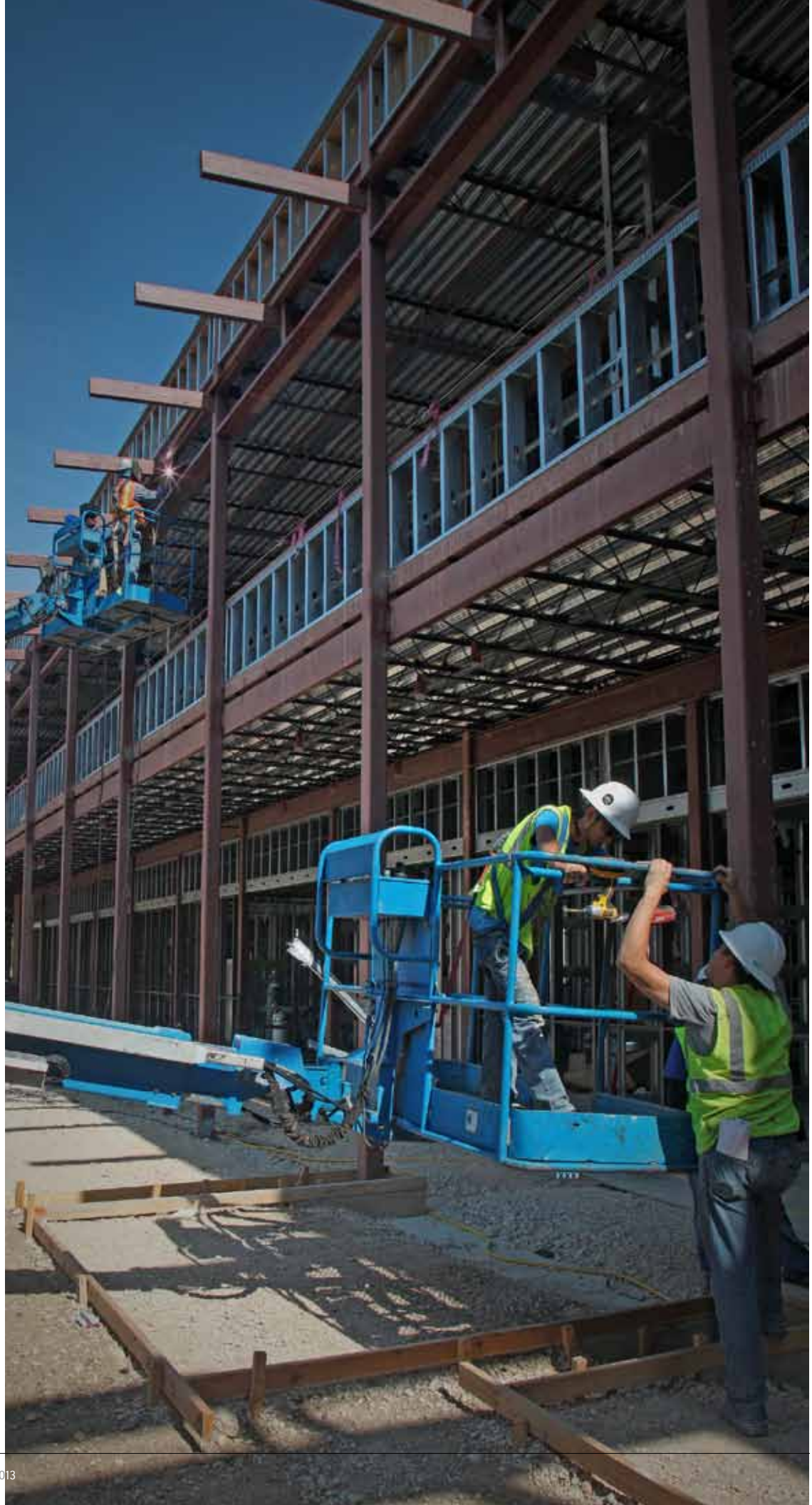
BUILDING UPDATE

By August 2013 the exterior walls, roof, many of the glass windows, interior walls and mechanical units had been installed in Texas Biomed's new 70,000-square-foot laboratory and office complex. Looking ahead to early 2014, the 15 new research laboratories will be home to Texas Biomed scientists and growing research programs. Named the Earl Slick Research Center after the brother of Texas Biomed founder Tom Slick, the $26.5 million facility is part of a campus master plan that includes a major effort to bring additional world-class scientists and new research programs to the Institute. Having raised some $33.5 million in gifts, Texas Biomed is currently focused on recruiting new scientists (see story on page 5) and developing new scientific initiatives that build on its many strengths. The goal of these efforts will be to promote the translation of discoveries into medical applications.



LETTER FROM THE PRESIDENT

DEAR FRIENDS,

THE OPPORTUNITY TO MAKE A PROFOUND DIFFERENCE IN THE LIVES OF OTHERS COMES ABOUT RARELY. YET, AT THE TEXAS BIOMEDICAL RESEARCH INSTITUTE, OUR SCIENTISTS ARE CONDUCTING A VARIETY OF RESEARCH PROJECTS THAT ARE GOING TO IMPACT THE HEALTH CARE OF PEOPLE HERE IN SAN ANTONIO AND AROUND THE WORLD FOR DECADES TO COME.

Take, for instance, the discovery by Dr. Laura Cox and her colleagues of four genes that are implicated in high levels of low density lipoprotein, the bad form of cholesterol. Interventions targeting those genes could well lead to better control over heart and circulatory illness.

Or a new project by Dr. John Blangero, funded by the Stevens Foundation, which involves identifying biomarkers for Parkinson's disease, a critical step in the early identification of persons at risk for this debilitating, and sometimes life-threatening, illness.

The work of Dr. Andrew Hayhurst is focused on improved screening techniques for a variety of pathogenic agents, including the many strains of botulism toxin, which naturally threaten our food supply, but which also could be used as a biothreat.

And the new studies of bats by Drs. Jean Patterson, Anthony Griffiths, and Ricardo Carrion Jr., and their colleagues are addressing the capacity of these animals to serve as reservoirs for several infectious diseases that threaten both humans and other animals.

Texas Biomed is an important player on the world stage of science and medicine. Novel and important findings are an everyday occurrence as these examples demonstrate. Yet, we must do more to get these discoveries transferred to the medical marketplace where they can be evaluated and, when appropriate, incorporated into new diagnostics, treatments and preventatives.

This process of identifying, protecting and then marketing intellectual property is called technology transfer. We must do more of it, because it is the vehicle by which discoveries get to the patient bedside and provide additional revenue for our research endeavors. Furthermore, we are actively seeking industry partners to collaborate with us, both on individual research projects and on multiyear, multi-investigator strategic alliances on such topics as diabetes, vaccine development, and arthritis. Such arrangements will diversify our sources of revenue, an important consideration in this era of sequestration, and accelerate the medical use of our discoveries. And they will not change the nature of the work being undertaken here.

Building upon an outstanding record of research accomplishment, and by creatively pursuing promising avenues of scientific inquiry, we will continue our leadership role and make the difference in people's lives that is our mission.

Thank you for all that you do to help us achieve these goals.

Sincerely,

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

"TEXAS BIOMED IS AN *important player* ON THE WORLD STAGE OF SCIENCE AND MEDICINE ... WE MUST DO MORE TO GET THESE DISCOVERIES *transferred to the medical marketplace*..."

LETTER FROM THE CHIEF SCIENTIFIC OFFICER

DEAR FRIENDS AND COLLEAGUES,

WHILE THE NEW EARL SLICK RESEARCH CENTER WILL BE VITAL TO INCREASING TEXAS BIOMED'S CAPACITY FOR SCIENTIFIC DISCOVERIES, IT IS THE SCIENTISTS AT TEXAS BIOMED WHO MAKE THOSE DISCOVERIES A REALITY TODAY. I AM DELIGHTED TO REPORT THE RECRUITMENT OF THREE WORLD-CLASS SCIENTISTS WHO WILL COMPLEMENT AND STRENGTHEN OUR EXISTING RESEARCH PROGRAMS AS WE ELEVATE TEXAS BIOMED TO THE NEXT LEVEL OF EXCELLENCE.

Robert Davey, Ph.D., Scientist and Ewing Halsell Scholar, was recruited from the University of Texas Medical Branch at Galveston to our Department of Virology and Immunology in August of 2011. Since his arrival, he has expanded his creative research program for screening thousands of drugs and other compounds for evidence of activity against pathogenic viruses. Although these compounds were not developed as antiviral drugs, Davey already has identified more than 500 of them that have antiviral effects and might be repurposed to treat viral diseases.

Davey also is investigating the biological mechanisms by which viruses gain entry into host cells. An understanding of those mechanisms may enable the development of novel drugs that block viral entry into cells, thereby preventing disease progression. Recently, Davey has begun taking advantage of our primate resources and will be testing a new disease model for Crimean-Congo hemorrhagic fever virus in marmosets, for which he was awarded a pilot grant from the Southwest National Primate Research Center. He plans to expand this program to test antiviral drugs in other nonhuman primates.

Ruth Ruprecht, M.D., Ph.D., Scientist and Director of the Texas Biomed AIDS Research Program, was recruited from the Dana-Farber Cancer Institute and Harvard Medical School to the Department of Virology and Immunology on July 1, 2013. Ruprecht has been a pioneer in research in AIDS vaccines since AIDS emerged as a new disease in the early 1980s. She also conducts research on the prevention of transmission of HIV from mothers to babies. She uses monkeys in both of these research programs. Texas Biomed has had an AIDS research program involving monkeys since the 1980s, and Ruprecht has brought new scientific strength and leadership to that program while enhancing its capacity to contribute directly to improving human health.

Michael Olivier, Ph.D., Scientist, was recruited from the Medical College of Wisconsin to the Department of Genetics on July 1, 2013. For more than three decades, the Department of Genetics has focused considerable attention on the identification of genes in which variation contributes to susceptibility or resistance to complex diseases, such as cardiovascular disease. Olivier is a specialist in research on gene function, and he will lead the effort to figure out how these newly identified gene variants function in imparting susceptibility to specific complex diseases. An understanding of gene function is expected to lead to new therapies that can prevent disease in individuals who are genetically susceptible.

These additions to Texas Biomed's intellectual scientific powerhouse will contribute to our capacity to stay ahead of the curve and to continue moving the cutting edge of science forward as we have done for many decades.

Sincerely,

John L. VandeBerg, Ph.D.

"I AM DELIGHTED TO REPORT THE RECRUITMENT OF THREE WORLD-CLASS SCIENTISTS WHO WILL *complement and strengthen our existing research programs* AS WE ELEVATE TEXAS BIOMED TO THE NEXT LEVEL OF EXCELLENCE."

Texas Biomed recruits two scientists in genetics and virology

TWO DISTINGUISHED SCIENTISTS HAVE JOINED THE FACULTY OF TEXAS BIOMED, ADDING RESEARCH FIREPOWER TO THE AREAS OF GENETICS AND VIROLOGY.

Michael Olivier, Ph.D., is an expert in the study of genes and proteins and their role in human disease. Ruth Ruprecht, M.D., Ph.D., has a long-standing and creative program in AIDS-related research and vaccines, and also conducts research on breast cancer.

"These recruitments are key elements of our major effort to attract more top-level scientists to the institution, scientists who will add to our existing research programs, initiate new ones and accelerate the pace of discovery," said Kenneth P. Trevett, Texas Biomed's president and CEO.

GENES AND PROTEINS

Olivier joined the Medical College of Wisconsin in 2001 as an assistant professor. He was promoted to associate professor in 2004 and to full professor with tenure in 2009. In addition to his position as director of the Wisconsin Center of Excellence in Genomics Science, Olivier was co-director of the TOPS Center for Obesity and Metabolic Research at the Medical College of Wisconsin.

"His research ultimately will lead to new approaches for treating many disorders, including diabetes, obesity and heart disease," said Sarah Williams-Blangero, Ph.D., the Genetics Department chair.

"My lab is interested in the genetic and functional analysis of common human disorders, with a special interest in lipid abnormalities such as high blood cholesterol and triglyceride levels," Olivier said. "We are trying to determine how these factors contribute to cardiovascular disease risk, especially in obese individuals. I am also interested in other complications of obesity, such as fatty liver disease."

PROTEIN STUDIES

"I believe my background in technology, especially in proteomics – the analysis of proteins – can contribute to many ongoing Texas Biomed studies on both humans and baboons. We will be able to merge our tools and technologies with the outstanding resources and human as well as baboon study cohorts at Texas Biomed," he added.

Olivier's research has been published in high-profile journals such as *Nature*, *Science* and the *Proceedings of the National Academy of Sciences*.

A major research effort of Olivier's, which already includes collaborations with John Blangero, Ph.D., and other scientists at Texas Biomed, analyzes the metabolic syndrome in humans, a disorder characterized by obesity, insulin resistance, dyslipidemia and hypertension. Olivier is using both family-based, genome-wide analysis and candidate gene studies to identify the genetic alterations affecting lipid metabolism, plasma lipid levels and disease manifestations of these abnormalities, such as abdominal obesity and nonalcoholic fatty liver disease.

AIDS RESEARCH

Ruprecht directs a multi-institutional AIDS research program that involves collaborators in the United States, Europe and Africa. In addition, she has served as a consultant for the World Health Organization and the China Comprehensive International Program for Research on AIDS, as a member of the National Institute of Allergy and Infectious Diseases (NIAID) AIDS Research Advisory Committee and the NIAID Council, and as the U.S. chair of the US-Japan AIDS Panel.

"She is going to be a great addition to our research efforts," said Jean L. Patterson, Ph.D., the Virology and Immunology Department chair.

"We have discovered a new mechanism by which certain antibodies can prevent AIDS virus infection in monkeys," said Ruprecht. "Joining Texas Biomed gives my group a wonderful opportunity to collaborate closely with experts in primate medicine at the Southwest National Primate Research Center. Together, we can really accelerate progress."

SNAPSHOT

Ruth Ruprecht, M.D., Ph.D., Scientist, Department of Virology and Immunology, and Director of the Texas Biomed AIDS Research Program.

Previously with: Dana-Farber Cancer Institute and Harvard Medical School.

Background: Ruprecht has been a pioneer in research in AIDS vaccines since AIDS emerged as a new disease in the early 1980s. She also conducts research on the prevention of transmission of HIV from mothers to babies.

Michael Olivier, Ph.D., Scientist, Department of Genetics.

Previously with: Medical College of Wisconsin.

Background: Olivier, a specialist in research on gene function, will lead the effort to figure out how newly identified gene variants function in imparting susceptibility to specific complex diseases.

Ruprecht received a Ph.D. in human genetics from Columbia University in New York and an M.D. from the University of Miami School of Medicine. In 1984, she joined the Dana-Farber Cancer Institute and Harvard Medical School, where she was promoted to professor of medicine with tenure in 1999. In 2001, she received an honorary professorship from the Institute of Medical Biology, Chinese Academy of Medical Sciences, at the Peking Union Medical College.

Ruprecht's research has been published in many high-profile journals, including *Nature, Science, Nature Medicine* and the *Proceedings of the National Academy of Sciences*. ■

Texas Biomed Virologists Report Big Gains against Bioterror Threats

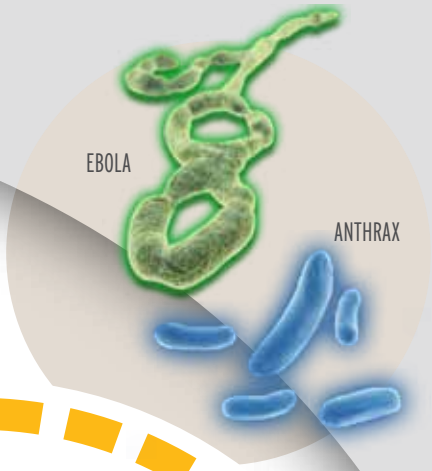
TEXAS BIOMED SCIENTISTS HAVE REPORTED TWO SIGNIFICANT RESEARCH ADVANCES IN THE CONTINUING FIGHT AGAINST THE POTENTIAL USE OF DEADLY PATHOGENS – SUCH AS ANTHRAX AND THE MARBURG AND EBOLA VIRUSES – IN BIOTERROR ATTACKS.

In the first study, Texas Biomed virologist Robert Davey, Ph.D., and his colleagues described the most extensive screen of its kind that demonstrated the feasibility of repurposing drugs already approved by the U.S. Food and Drug Administration (FDA) for use against these highly pathogenic agents.

In testing a library of 1,012 drugs used for treatment of everyday ailments like diabetes and high blood pressure, the scientists found that 10 were active against two or more bacteria and that 24 were active against two or more viruses.

Two drugs were found to be the most potent compounds in protecting mice against anthrax while one drug, chloroquine, once used to treat malaria, protected mice against Ebola virus, said Davey.

The new study, which included authors Jean Patterson, Ph.D., and Ricardo Carrion Jr., Ph.D., both of Texas Biomed, appeared in the journal *PLOS ONE*. The findings were the result of a collaborative effort among Texas Biomed, independent research institute SRI International and the U.S. Army Medical Research Institute of Infectious Diseases. It was supported by funds from the Defense Threat Reduction Agency, the Defense Department's agency for countering weapons of mass destruction.



DISCOVERY 1

USING EXISTING DRUGS TO FIGHT BIOTERROR

Scientists at Texas Biomed found 34 existing, FDA-approved drugs used for other treatments that were active against at least four bioterror bacteria and viruses.

Currently approved drugs are already known to be safe for patients and can be quickly made available for a new indication in an emergency.

Two of the drugs were found to protect mice against anthrax, while another, once used to treat malaria, protected mice against Ebola.

More work is needed before these methods could be used in people, as mice are not the best models for testing the drugs, and the drugs have significant side effects.

NEW USES FOR EXISTING DRUGS

"Repurposing of existing drugs that may have unanticipated activities as potential countermeasures is one way to meet this important goal, since currently approved drugs already have well-established safety and pharmacokinetic profiles in patients, and manufacturing and distribution networks," the authors wrote. "Therefore, approved drugs could rapidly be made available for a new indication in an emergency."

The scientists found a variety of hits against two or more of these biothreat pathogens, which were validated in secondary tests. As expected, antibiotic compounds were highly active against bacterial agents, but the researchers did not identify any nonantibiotic compounds with broad-spectrum antibacterial activity.

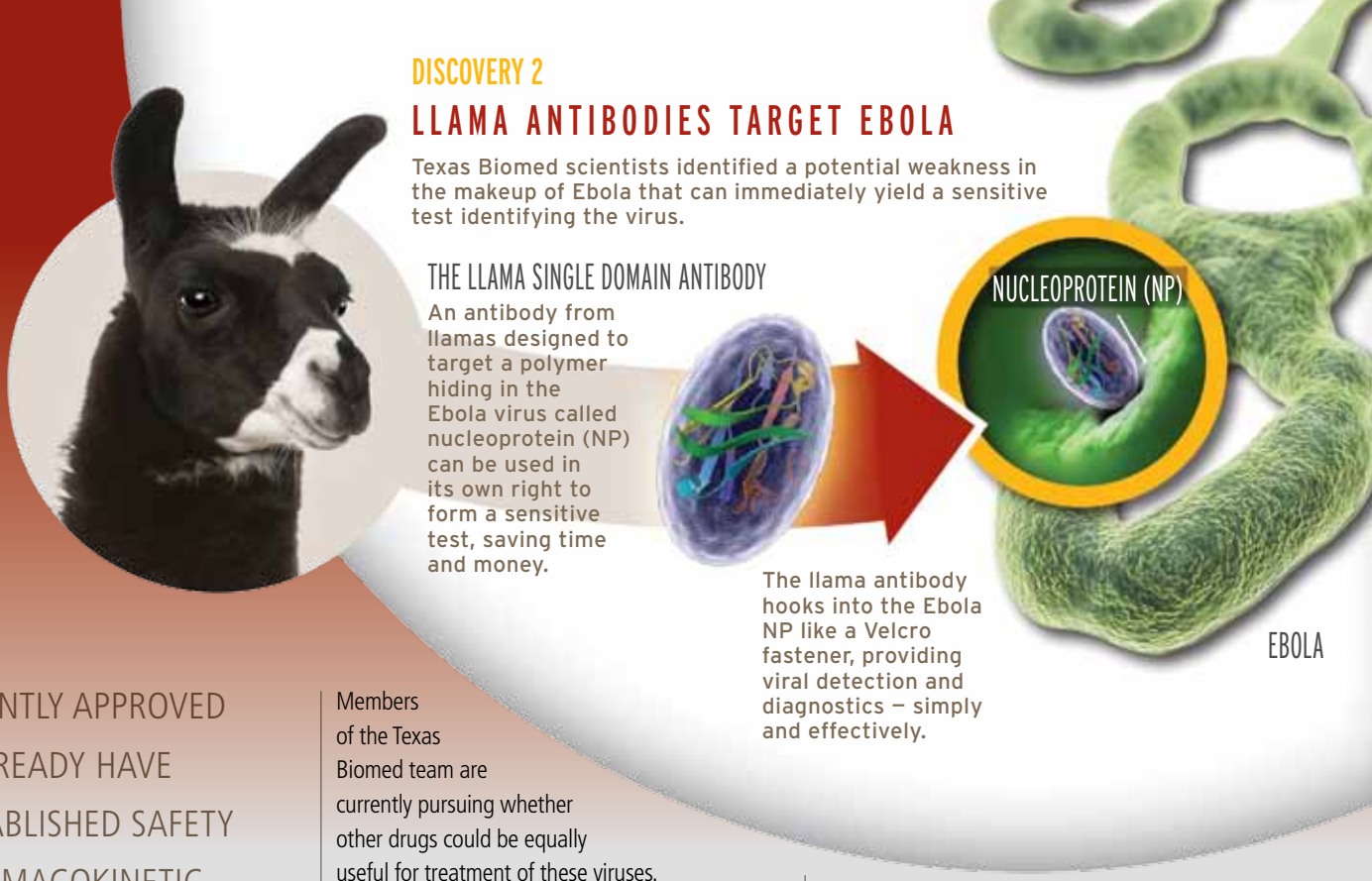
Lomeflaxacin and erythromycin were found to be the most potent compounds in protecting mice against anthrax. Lomeflaxacin is used to treat bronchitis and urinary tract infections. Erythromycin is used against respiratory tract infections.

The most noteworthy antiviral compound identified was chloroquine, which disrupted virus entry and replication in cells of two or

DISCOVERY 2

LLAMA ANTIBODIES TARGET EBOLA

Texas Biomed scientists identified a potential weakness in the makeup of Ebola that can immediately yield a sensitive test identifying the virus.



"... CURRENTLY APPROVED DRUGS ALREADY HAVE WELL-ESTABLISHED SAFETY AND PHARMACOKINETIC PROFILES IN PATIENTS, AND MANUFACTURING AND DISTRIBUTION NETWORKS. THEREFORE, APPROVED DRUGS *could rapidly be made available for a new indication in an emergency.*"

more viruses in vitro and protected mice against Ebola virus.

FASTER COUNTERMEASURES

Because of the complexity of working with these pathogens under laboratory conditions as well as the fact that human drug clinical trials cannot be ethically conducted for any of these agents, conventional drug discovery and development approaches are particularly challenging. For these agents, the FDA must evaluate the efficacy of drugs on the basis of the way they behave in appropriate animal models, under FDA guidance. Thus, drug-repurposing offers many advantages, particularly because human safety studies have already been conducted on them.

Members of the Texas Biomed team are currently pursuing whether other drugs could be equally useful for treatment of these viruses.

"It would be important to determine if a combination of drugs could be more potent than each individual drug," Davey said. "Such synergy, when seen, usually means you can lower the dose of each drug and still have a big impact on the disease while minimizing bad side effects. Such work could prove useful as an easy frontline defense against these viruses."

LLAMA ANTIBODIES AGAINST EBOLA

In another study, scientists screening a library of a billion llama antibodies on live Ebola viruses in Texas Biomed's highest biocontainment laboratory identified a potential weakness in the makeup of these deadly agents that can immediately yield a sensitive test for identifying the virus.

"Detecting single viral protein components can be challenging, especially at very low levels. However, most viruses are repetitive assemblies of a few components, called antigens, with some existing as polymers, which present highly 'avid' targets for antibodies," said Texas Biomed virologist Andrew Hayhurst, Ph.D.

"Think of one pair of microscopic Velcro hooks where one hook is the viral antigen and the other is the antibody and it is a weak interaction. Have a thousand pairs of hooks and it makes a very powerful interaction ... just like Velcro fasteners on hiking gear," Hayhurst explained.

The screening performed by Hayhurst and assistant Laura Jo Sherwood, B.S., guided the selection of llama antibodies recognizing a polymer hiding within Ebola called nucleoprotein (NP). Remarkably, each antibody could be used in its own right to form a sensitive test for the Ebola NP, whereas most tests would require two different antibodies, driving up costs and characterization times.

This research — funded by the National Institutes of Health, Defense Threat Reduction Agency Basic Science Program/Office of Naval Research and the Texas Biomedical Research Institute — was also published in the journal *PLOS ONE*.

"Ebola NP is rather like a cob of corn displaying hundreds of kernels linked in a repetitive polymer, giving us the perfect molecular magnet to attract llama antibodies that can be assembled into highly avid assays based on a single antibody," Hayhurst said.

"Intriguingly, while using one antibody to polymers and aggregates has been put to use in neurodegenerative disease diagnostics for Parkinson's, Alzheimer's and other disorders, it has lagged behind in emerging viral diagnostics. Our study showcases its simplicity and effectiveness for viral threat detection and it may well be useful for detecting other emerging viruses," he concluded. ■

Geneticists Identify Four Candidate Genes Related to 'Bad' Cholesterol

Scientists at Texas Biomed have identified four candidate genes that influence levels of "bad" cholesterol in baboons at the Southwest National Primate Research Center (SNPRC). This discovery ultimately could lead to the development of new drugs to reduce the risk of heart disease, the nation's number-one killer.

"Our findings are important because they provide new targets for the development of novel drugs to reduce heart disease risk in humans," said Laura Cox, Ph.D., a Texas Biomed geneticist. "Since these genes have previously been associated with cancer, our findings suggest that genetic causes of heart disease may overlap with genetic causes of some types of cancer."

The new study, funded by the National Institutes of Health, was published in the *Journal of Lipid Research*. Other Texas Biomed scientists on the study include Genesio Karere, Ph.D.; Jeremy Glenn, B.S.; Shifra Birnbaum, B.S.; Michael Mahaney, Ph.D.; and John L. VandeBerg, Ph.D.

The Texas Biomed researchers screened the colony of 1,500 baboons at the SNPRC and found three half-siblings with low levels of low density lipoprotein (LDL) — the "bad" cholesterol — and three half-siblings with high levels of LDL. These animals were then fed a high-cholesterol, high-fat diet for seven weeks.

Cox and her colleagues used gene array technology and high-throughput sequencing to home in on the genes expressed in the two groups and differentiate those in the low LDL group from those in the high LDL group. They discovered that four genes (named *TENC1, ERBB3, ACVR1B* and *DGKA*) are associated with LDL levels. Interestingly, these four genes are part of a signaling pathway important for cell survival, the disruption of which promotes some types of cancer.

HEART DISEASE RISK

It is well known that a high level of LDL cholesterol is a major risk factor for heart disease. Despite concerted efforts for the past 25 years to manage cholesterol levels through changes in lifestyle and treatment with medications, heart disease remains the leading cause of death and mortality in the United States and around the world. It will account for one out of four U.S. deaths in 2013, according to the American Heart Association.

Heart disease is a complex disorder thought to be a result of interactions between genetic and environmental factors. To understand why humans have different levels of LDL and thus vary in risk for heart disease, the genetic factors causing these differences need to be understood.

"OUR FINDINGS ... PROVIDE NEW TARGETS FOR THE DEVELOPMENT OF NOVEL DRUGS TO *reduce heart disease risk in humans.*"

— LAURA COX, PH.D.

BABOON STUDIES

Texas Biomed scientists are using baboons in their research on heart disease. These animals are similar to humans in their physiology and genetics; also, investigators are able to control their dietary intake, which is very difficult to do in humans. The characteristics of the baboon model provide investigators with unique opportunities to identify genes that influence heart disease risk.

The new research also suggests that knowing many of the genes responsible for heart disease may be necessary to devise effective treatments. For example, several genes may need to be targeted at the same time to control risk.

"The next step in this research is to find the mechanism by which these genes influence LDL cholesterol," Cox said. "That starts to give us the specific targets for new therapies."

If all goes well, this information may be available within two years. ■

THE STUDY

1 Texas Biomed researchers screened the colony of baboons at the SNPRC and found three half-siblings with low levels of low density lipoprotein (LDL) – the "bad" cholesterol – and three half-siblings with high levels of LDL.

2 These animals were then fed a high-cholesterol, high-fat diet for seven weeks.

3 Through gene testing, the scientists sought to differentiate those in the low LDL group from those in the high LDL group.

4 They discovered that four genes are associated with LDL levels. Interestingly, these four genes are part of a signaling pathway important for cell survival, and disruption of this pathway promotes some types of cancer.

New Drug for Hepatitis B Could Transform Treatment

A NOVEL DRUG DEVELOPED BY GILEAD SCIENCES AND TESTED IN AN ANIMAL MODEL AT TEXAS BIOMED SUPPRESSES HEPATITIS B VIRUS INFECTION BY STIMULATING THE IMMUNE SYSTEM AND INDUCING LOSS OF INFECTED CELLS. THE NEW THERAPY REPRESENTS THE FIRST CONCEPTUALLY NEW TREATMENT FOR HEPATITIS B VIRUS (HBV) IN MORE THAN A DECADE AND COULD BE TRANSFORMATIVE IN TREATING THIS DISEASE.

In a study conducted at Texas Biomed's Southwest National Primate Research Center, researchers found that the immune modulator GS-9620, which targets a receptor on immune cells, reduced both the virus levels and the number of infected liver cells in chimpanzees chronically infected with HBV. Because chimpanzees are the only species other than humans that can be infected by HBV, the results from this study were critical in moving the drug forward to human clinical trials, which are now in progress.

The new report, co-authored by scientists from Texas Biomed and Gilead Sciences, appeared in the journal *Gastroenterology*. Gilead researchers had previously demonstrated that the same therapy could induce a cure of hepatitis infection in woodchucks that were chronically infected with a virus similar to human HBV.

NEW THERAPY STIMULATES THE IMMUNE SYSTEM

"This is an important proof-of-concept study demonstrating that the therapy stimulates the immune system to suppress the virus and eliminate infected liver cells," said co-author Robert E. Lanford, Ph.D., of Texas Biomed. "One of the key observations was that the therapy continued to suppress virus levels for months after therapy was stopped."

The current therapy for HBV infection targets the virus and works very well at suppressing viral replication and delaying progression of liver disease, but it is a lifelong therapy that does not provide a cure.

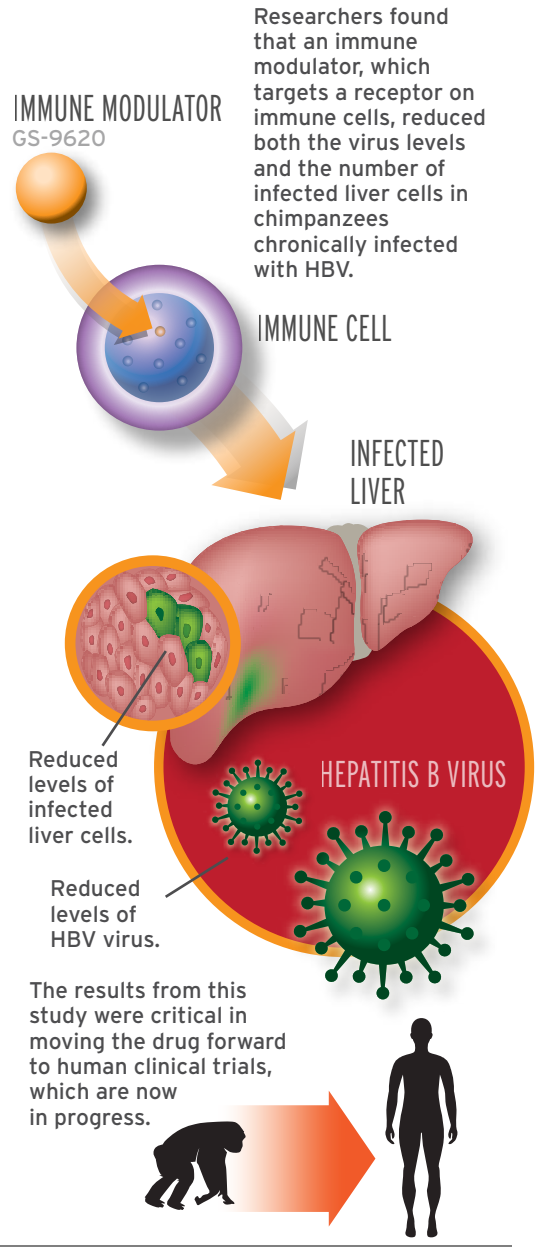
The Gilead drug binds a receptor called Toll-like Receptor 7 that is present in immune cells. The receptor normally recognizes invading viruses and triggers the immune system to suppress viral replication by the innate immune response and kill infected cells by the adaptive immune response, thus orchestrating both arms of the immune system.

"ONE OF THE KEY OBSERVATIONS WAS THAT THE THERAPY *continued to suppress virus levels for months after therapy was stopped.*"

— ROBERT E. LANFORD, PH.D.

HBV damages the liver, leading to cirrhosis and liver cancer. Liver cancer is the fifth most common cancer worldwide and the third most common cause of cancer death. According to the U.S. Centers for Disease Control and Prevention, up to 1.4 million Americans are chronically infected with HBV. The World Health Organization estimates that two billion people have been infected with the hepatitis B virus, resulting in more than 240 million people with chronic infections and 620,000 deaths every year. ■

THE FINDING



Standwell Nkhoma: Fighting malaria in Africa with training at Texas Biomed

Between the ages of 4 and 12, growing up in a grass hut in the village of Chifira, Malawi, Standwell Nkhoma, a scientist in the Department of Genetics, struggled through three bouts of malaria virtually every year. He frequently missed months of school at a time in order to overcome the high fever, headache, vomiting and other symptoms of this mosquito-borne disease.

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.

The economy in Malawi, a former British colony, is based on agriculture, and its mostly rural population is often difficult to reach with the latest measures to prevent and treat malaria and other all-too-common diseases such as HIV/AIDS and tuberculosis.

Nkhoma was so determined to fight the scourge of malaria that has afflicted virtually all of his 15 million countrymen, including his five brothers and parents, that he decided to use his acuity for mathematics and science to pursue new ways to overcome this disease.

"HE'S TAKING THE EXPERTISE HE GAINED HERE BACK TO HIS HOME COUNTRY TO BUILD SCIENTIFIC INFRASTRUCTURE THERE, AND *will continue expanding our network of collaborations.*"

— SARAH WILLIAMS-BLANGERO, PH.D.

SNAPSHOT

Standwell Nkhoma, a scientist in the Department of Genetics, is leading a new research project to understand the biology of malaria and improve treatment and surveillance in his native continent, expected to improve the understanding of the complex relationship between parasites and the people they infect.

Nkhoma graduated from the University of Malawi in 1999 and earned a Ph.D. in chemistry in a program at the University of Liverpool sponsored by the Gates Malaria Partnership and the Wellcome Trust in 2005.

Nkhoma was so determined to fight the scourge of malaria that has afflicted virtually all of his 15 million countrymen, including his five brothers and his parents, that he decided to use his acuity for mathematics and science in the pursuit of new ways to overcome this disease.

Nurses screen for malaria at an outpatient clinic in Malawi.

He graduated from the University of Malawi in 1999 and earned a Ph.D. in chemistry in a program at the University of Liverpool sponsored by the Gates Malaria Partnership (GMP) and the Wellcome Trust in 2005. Nkhoma did a postdoctoral research project sponsored by GMP and then came to Texas Biomed late in 2008 to expand his knowledge and skills in the genetics of malaria drug resistance with Tim Anderson, Ph.D.

NEW GRANT TO UNDERSTAND MALARIA

Now 37 years old, Nkhoma is leading a new research project funded by a major four-year, $700,000 grant from Britain's Wellcome Trust to understand the biology of malaria and improve treatment and surveillance in his native continent.

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

Added Anderson: "Standwell is doing this with the support of a very prestigious grant. That's a great positive story about the global impact of Texas Biomed."

The grant will enable Nkhoma to perform field work 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."

A DAUNTING CHALLENGE

Patients have been known to have as many as 14 different parasites per infection. Nkhoma will use new methods developed in the Anderson laboratory at Texas Biomed by Ian Cheeseman, Ph.D., and Shalini Nair that allow genotyping and even genome sequencing of single infected blood cells. By examining single cells, he will be able to describe the different malaria parasites within a single patient in unprecedented detail.

"Knowing this won't wipe out infection," Nkhoma said. "But it is very crucial for us to understand the biology of the parasite – how it reacts with the human body and immune system, and how different variants interact in the same patient."

The interactions between different parasites within infections have been shown to increase disease severity in mice, but the phenomenon is far from understood. Nkhoma will investigate this question in human malaria infections. He plans to study 100 patients divided into three groups: those with the parasite in their bloodstream but without symptoms; those with mild symptoms; and those with severe malaria that affects the brain and causes coma.

Nkhoma's research project is expected to improve the understanding of fundamental aspects of the complex relationship between parasites and the people they infect. Such knowledge is urgently required and will contribute to global efforts to eliminate this disease. ■

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CAMPUS BRIEFS

High School Teachers' Day

Texas Biomed hosted a day on the campus on June 18 for 50 Bexar County area high school science teachers. The day-long program, which focused on class preparation for the teachers and included posters, curricular materials and a classroom laboratory demonstration kit, was sponsored by a grant from Silver Eagle Distributing Inc. Jerilyn Pecotte, Ph.D., organized the day's events, which included a warm welcome from Texas Biomed President Kenneth P. Trevett and a briefing by Vice President for Institutional Advancement Corbett Christie. Tours of research laboratories, the DNA sequencing center, the Southwest National Primate Research Center and the AT&T Genomics Computing Center gave the teachers a close-up view of today's biomedical research. The afternoon featured presentations on current research projects by faculty members Tim Anderson, Ph.D., Melanie Carless, Ph.D., Marie-Claire Gauduin, Ph.D., Andrew Hayhurst, Ph.D. and John Bernal, D.V.M.

Texas Biomed's Anderson a Health Care Hero

Texas Biomed's Tim Anderson, Ph.D., a scientist in the Department of Genetics, has been designated a Health Care Hero by the *San Antonio Business Journal*. The annual award honors leaders in the city's health care and biomedical fields.

"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," said Sarah Williams-Blangero, Ph.D., Genetics Department chair.

Malaria killed 655,000 people — more than one per minute — in 2010. While these numbers are high, malaria deaths have declined by 30 percent over the past decade, largely because of treatment with combination therapies containing artemisinin, a plant-derived antimalarial drug developed in China.

However, Anderson and his collaborators recently documented the emergence of resistance to artemisinin in western Thailand, which represents 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 there will soon be effective molecular markers for monitoring the spread of resistance.

Texas Biomed receives Stevens Grant

The Perry & Ruby Stevens Charitable Foundation of Kerrville, Texas, has 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. Directed by John Blangero, Ph.D., the research will incorporate members of the San Antonio Family Study population, which is well characterized and has whole genome sequence data available for participants. Parkinson's disease, 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 neurotransmitter. At least 30 percent to 40 percent of the variability in risk of Parkinson's disease is due to genetic factors.