TEXAS BIOMEDICAL RESEARCH INSTITUTE

FALL 2012

PROGRESS

Enhancing lives through discovery™

Fighting Malaria

Researchers home in on genes causing malaria drug resistance, critical information as resistance spreads in S.E. Asia

PAGE 6

INSIDE:

Groundbreaking starts work on Texas Biomed's Earl Slick Building

PAGE 3

LETTER FROM THE PRESIDENT

DEAR FRIENDS,

WHILE I RECEIVE MANY POSITIVE COMMENTS ABOUT TEXAS BIOMED, I AM SOMETIMES ASKED JUST WHAT ARE THE SPECIFIC ACCOMPLISHMENTS ACHIEVED BY THIS ORGANIZATION THAT HAVE CHANGED, OR ARE CHANGING, THE COURSE OF MEDICAL CARE. IT IS A FAIR QUESTION — AFTER ALL, OUR MISSION IS TO "IMPROVE THE HEALTH OF OUR GLOBAL COMMUNITY THROUGH INNOVATIVE BIOMEDICAL RESEARCH."

"THE NEW BUILDING IS... ABOUT INCREASING OUR...CAPACITY *to impact public health*. THE EARL SLICK BUILDING ALLOWS US TO RECRUIT NEW FACULTY WHO WILL *help us find answers to a variety of life-threatening and life-altering conditions*."

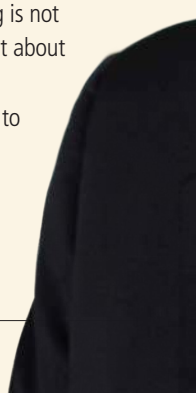
Briefly looking back, I consider just some of the major accomplishments to include:

- Development of the baboon as a model of heart and circulatory diseases, an extremely important advance which has played a key role in the fifty percent decline since 1960 in mortality caused by these common and deadly illnesses;
- Invention of the high frequency ventilator and proving the efficacy of artificial surfactants, each of which has contributed to reducing the death rate of significantly premature infants;
- Demonstration of the safety and efficacy of the hepatitis B vaccine, now used across the globe, and participation in the development of new, and far less toxic, treatments for hepatitis C; and
- Creation of SOLAR, a novel software for human genetic analysis, which is used internationally by 5,000 researchers and is helping to usher in a new era of personalized medicine.

The future, however, belongs to those who stay ahead of their fields, who have the courage to challenge established dogma and who are not afraid to aggressively pursue the most complex biological and pathological mysteries. Current research at Texas Biomed which likely will translate into better preventatives, diagnostics and treatments — perhaps even cures — includes:

- Genetic analysis of the causation for depression, a profoundly important public health problem that affects one in five adults in the United States, which may lead to a definitive diagnostic tool and new therapies;
- Advances in vaccine development against filoviruses such as Ebola and Marburg, potential bioterrorist weapons as well as the causative agents of lethal diseases in certain parts of the developing world;
- The development of an animal model for non-alcoholic fatty liver disease, a condition affecting up to 15 million Americans, an important step in addressing the most prevalent liver illness in the United States; and
- A disturbing discovery that people in Western Thailand may be developing resistance to the most common drug against malaria, portending a possible international increase in the number of deaths caused by this major killer. However, the same research group has identified a region of the malaria parasite genome associated with this drug resistance, thereby raising hope that there will soon be effective molecular markers for monitoring the spread of resistance.

As Texas Biomed constructs its new laboratory and scientific support facility, the Earl Slick Building, the value of this institution to the health of the world cannot be over-estimated. Its contributions to basic and translational science open the door to new approaches to disease management, both here and abroad. The new building is not about growth for the sake of growth, but about increasing our capacity to impact public health. The Earl Slick Building allows us to recruit new faculty who will help us find answers to a variety of life-threatening and life-altering conditions.



Phyllis Slick Cowell, daughter of Earl Slick, and her family at the groundbreaking on May 24. From left, John Cowell, Phyllis Slick Cowell, Maile Cowell, Lynn Ives, Jane Ives, Allen Ives and Michelle Cowell.

We can do more…we should and we will. You are giving us the tools to do just that. Thank you for sharing our vision for a healthier future and a more stable and secure planet.

Sincerely,

Kenneth P. Trevett, J.D.

Texas Biomed Starts New Laboratory and Office Complex; Announces Public Phase of Capital Campaign

Texas Biomed's new 70,000 square-foot laboratory and office complex will be named the Earl Slick Building, to honor the brother of Tom Slick, who played a critical role in the development of Texas Biomed during his lifetime and whose generosity, and that of his family, continues to positively impact the organization. Groundbreaking occurred on May 24 for the new facility which is part of a campus master plan that includes a major effort to recruit more world-class scientists, enhance existing research programs and initiate new ones to accelerate the pace of discovery at Texas Biomed.

"A transformational expansion of the Texas Biomed campus will soon become a reality," said J.R. Hurd, chair of Texas Biomed's board of trustees. "Thanks to the work of our architects — Lake Flato and FKP Architects — our new laboratory complex will make a compelling statement about the vision and energy of our institution. As our research programs blossom and grow, it reaffirms we are on the right track to improving human health worldwide."

Having raised some $30 million in gifts during the previous 18 months, Texas Biomed also announced the public phase of a capital campaign to raise another $11 million by the time of

Continued on page 4

The new, $25 million Earl Slick Building will be the largest in the history of the Institute, provide an attractive "front door" for Texas Biomed and represent the public face of the campus.

George C. Hixon, a former Texas Biomed board of trustees chair, at the wheel of the front loader at the groundbreaking.

Continued from page 3

the completion of the laboratory building in early 2014. "Time and time again, our supporters — our family if you will — have provided the life blood that is so critical to our success," said John Kerr, campaign co-chair. "While we have achieved this first goal in the quiet phase of our campaign, the support of our trustees and lead donors speaks loudly."

To enhance existing programs and start new ones, the plan is for a total of six new faculty members for the Genetics Department and Virology and Immunology Department. A new director and a junior faculty member also will be recruited for the Southwest National Primate Research Center (SNPRC). The goal of these recruitments will be to promote the translation of discoveries into medical applications.

Texas Biomed also plans to develop a regenerative medicine program to advance the effort to replace dead or dying tissue in people with a variety of conditions and illnesses. This effort, which will involve recruiting two additional researchers, will include collaborations with other investigators and research institutions in San Antonio.

The new, $25 million Earl Slick Building will be the largest in the history of the Institute, provide an attractive "front door" for Texas Biomed and represent the public face of the campus.

SNAPSHOT:

Project: 70,000 square foot campus expansion
Cost: $25 million
Features: The laboratory and office building will consist of 15 research laboratories, shared instrument rooms for these laboratories, and equipment and service space. The complex also will consolidate researchers and laboratories now housed in multiple buildings around the campus and will substantially increase efficiency of research through shared staff and equipment.

The laboratory and office building will consist of 15 research laboratories, shared instrument rooms for these laboratories, and equipment and service space. The complex also will consolidate researchers and laboratories now housed in multiple buildings around the campus and will substantially increase efficiency of research through shared staff and equipment.

In addition, the building will provide space for a number of nationally prominent visiting scientists who will collaborate with Texas Biomed researchers. And, it will serve as a visible focal point for the SNPRC, one of only eight such centers in the United States and the only one in the Southwest.

The design of the new headquarters honors the Slick legacy and adds a new level of detail and artistry to the campus with its use of tilt-wall construction for the new building's facades. The building's shape, orientation, and systems also work together integrally to reduce overall energy use. Current projections show the new structure will operate at 20 percent better efficiency than current building codes require. This energy efficiency — combined with other environmentally appropriate decisions with respect to the site design, water consumption, building materials and indoor environmental quality — has the project tracking to achieve certification from the U.S. Green Building Council's Leadership in Energy and Environmental Design rating system.

The designers of the building are Lake Flato Architects of San Antonio and FKP Architects of Houston. The construction manager is Vaughn Construction.

The Earl Slick Building is part of a campus master plan which envisions projects that will address needs far into the future — as much as 25 years — a significant planning horizon, considering the blistering pace of innovation in science.

The plan includes support infrastructure — engineering, energy, utilities, communications, and transportation — and provides more open, green, and pedestrian-friendly spaces. It will result in a rearrangement of the campus, with a new entrance and new courtyard and common areas that will make Texas Biomed a more aesthetically pleasing place to work and visit. ■

Research Institutions Join Forces To Develop Vaccines

TEXAS BIOMED AND THREE OF SAN ANTONIO'S OTHER LARGE RESEARCH INSTITUTIONS HAVE JOINED FORCES TO DEVELOP NEW VACCINES IN A PARTNERSHIP CALLED THE SAN ANTONIO VACCINE DEVELOPMENT CENTER.

"This collaboration will focus on vaccine development, not just the study of the basic biology of disease processes. It is a virtual center so funds received will be used entirely for research and development, including the procurement of specialized equipment to conduct this work," said Texas Biomed President Kenneth P. Trevett at a City Hall news conference in April.

All four institutions — UT Health Science Center San Antonio, University of Texas at San Antonio, the Southwest Research Institute and Texas Biomed — already have vaccine research under way.

Among the early accomplishments of the Center are the:

- Creation of an operating framework contained in a memorandum of understanding between the four partner institutions.
- Start-up of a pilot grant program for scientists at the participating institutions, with an emphasis on collaborative projects between scientists at two or more of the institutions.
- Establishment of an annual vaccine symposium, with the first such program to take place at the UT Health Science Center Greehey Children's Cancer Research Institute on November 16, 2012.

"IT IS A VIRTUAL CENTER SO FUNDS RECEIVED *will be used entirely for research and development*, INCLUDING THE PROCUREMENT OF SPECIALIZED EQUIPMENT TO CONDUCT THIS WORK."

— KENNETH P. TREVETT

- Commencement of planning for cooperative submissions to funding agencies.

The group has raised $600,000 in private donations — including a corporate gift from USAA and a personal donation from NuStar Energy LP Chairman Bill Greehey. The group has applied for another $300,000 from the Texas Research Incentive Program, a state fund that provides a 50 percent match for private gifts of up to $1 million to emerging research universities such as UTSA. Additional grant funds are expected to follow.

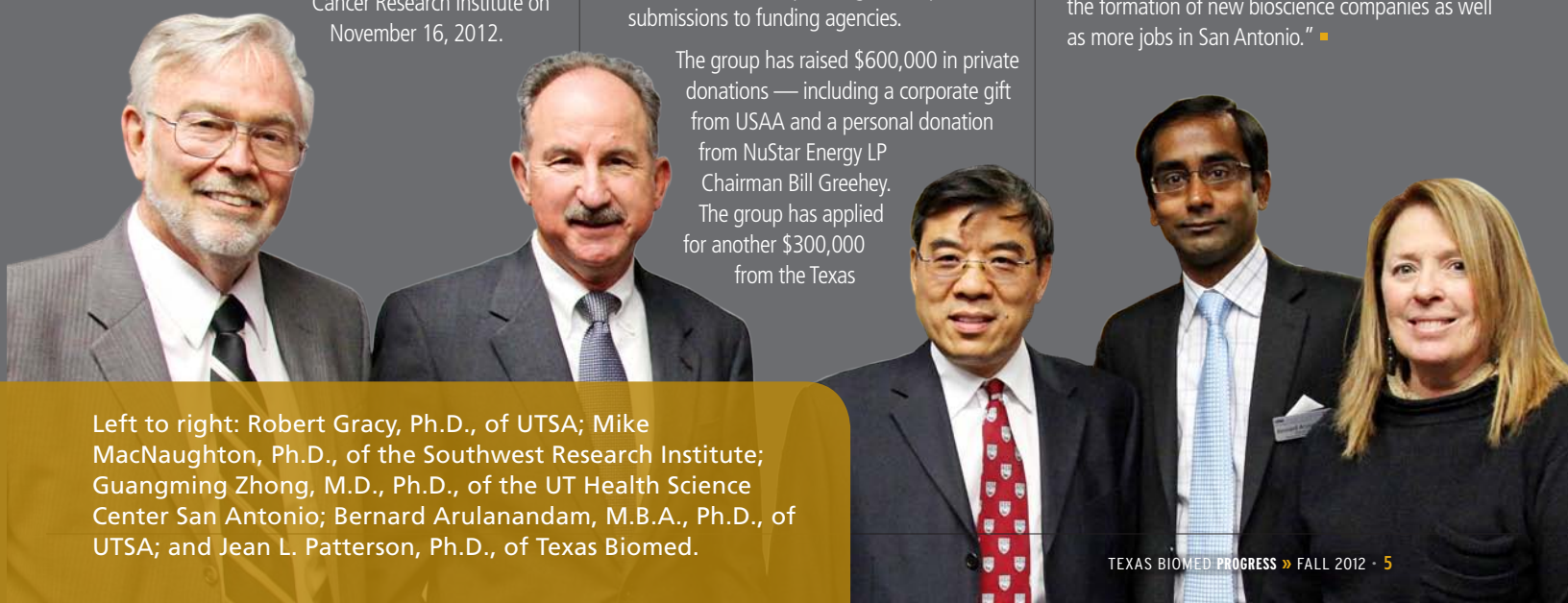
Initially, four to five grants of up to $50,000 each will be awarded to researchers from among the four partners, with priority given to collaborations between two or more of the institutions.

"Resources include small and large animal modeling, biocontainment laboratories, the science of genomics, using genetic techniques to create new vaccines, high throughput screening of vaccine candidate antigens and efficient systems to deliver vaccines and enhance effectiveness in humans," said Bernard Arulanandam, Ph.D., associate dean for research at UTSA. His work includes development of an experimental chlamydia vaccine in collaboration with scientists at the Health Science Center.

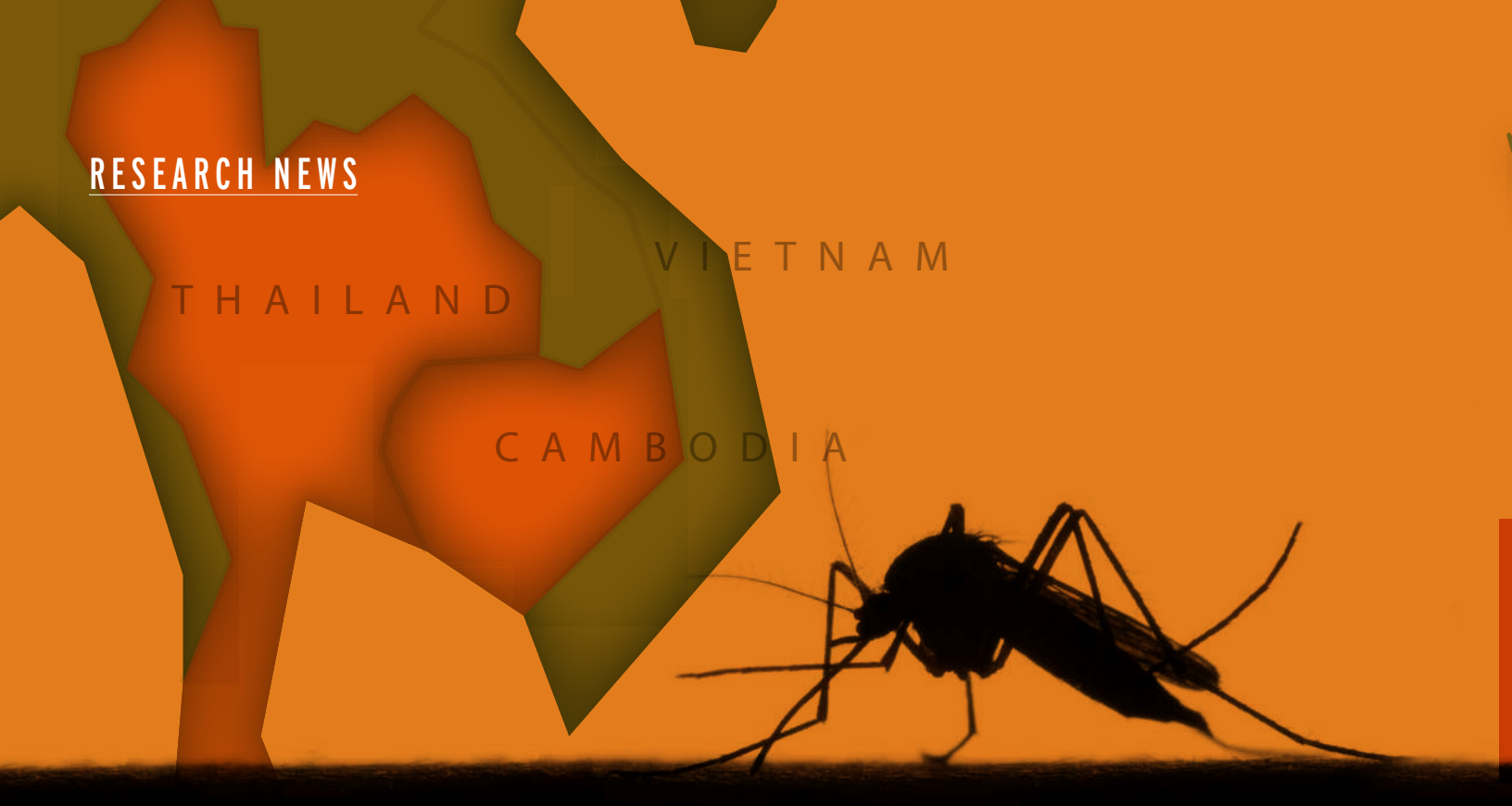
Other projects will include vaccines now under development at Texas Biomed against tularemia and Lassa virus, both potential bioterror threats, and vaccine delivery systems at the Southwest Research Institute.

Ann Stevens, president of BioMed SA, praised the new effort: "Infectious disease research is one of five areas we have identified where San Antonio has recognized strengths of national or international caliber," she said.

The partnership drives more innovation and creativity, said City Manager Sheryl Sculley, that " … in turn can create health solutions and products that can be commercialized, and result in the formation of new bioscience companies as well as more jobs in San Antonio." ■



Left to right: Robert Gracy, Ph.D., of UTSA; Mike MacNaughton, Ph.D., of the Southwest Research Institute; Guangming Zhong, M.D., Ph.D., of the UT Health Science Center San Antonio; Bernard Arulanandam, M.B.A., Ph.D., of UTSA; and Jean L. Patterson, Ph.D., of Texas Biomed.



Texas Biomed Studies Describe Setbacks and Advances in Global Malaria Fight

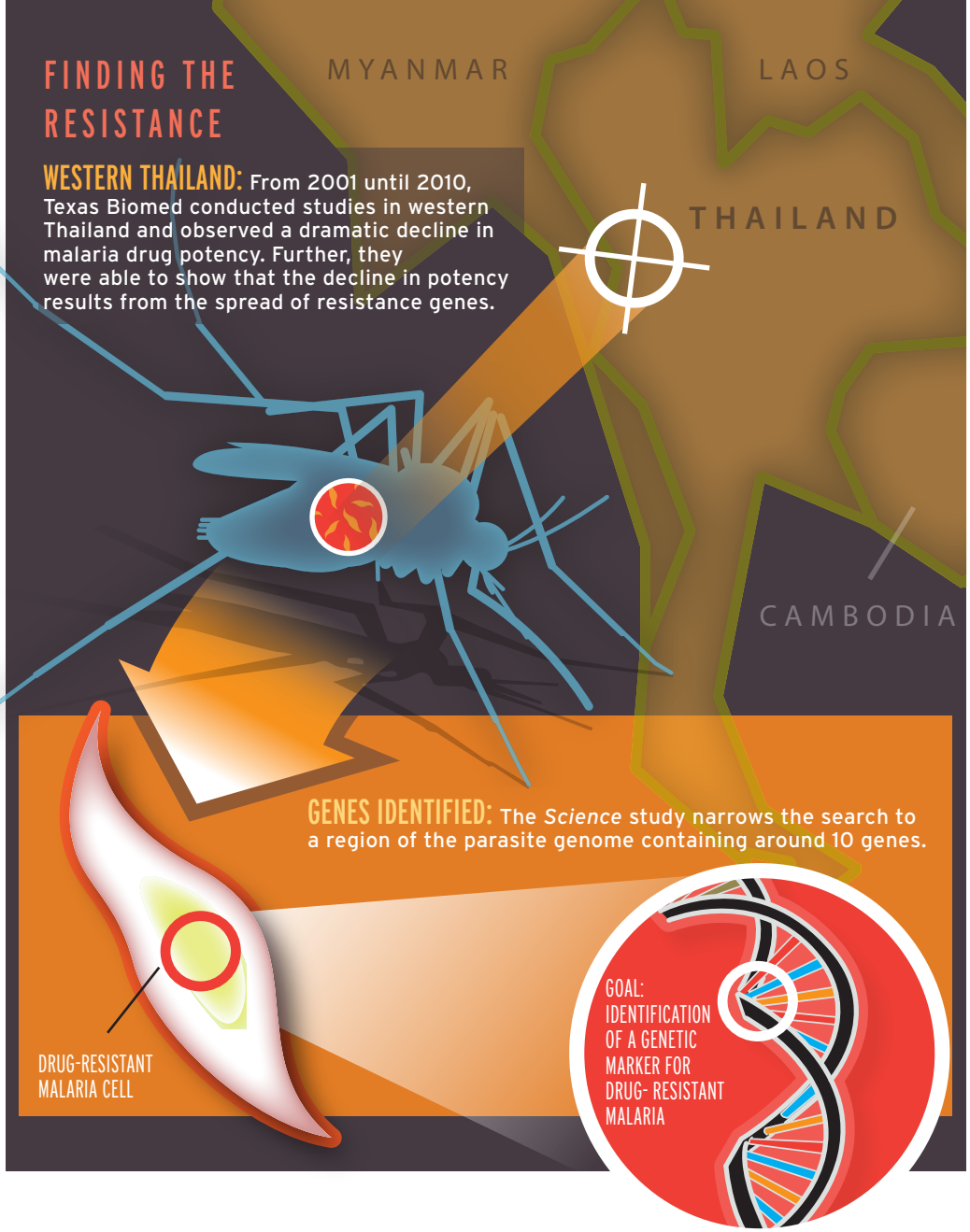
EMERGENCE OF RESISTANCE TO THE DRUG ARTEMISININ IN WESTERN THAILAND HAS CREATED A CRITICAL POINT IN GLOBAL EFFORTS TO CONTROL AND ELIMINATE MALARIA WORLDWIDE, ACCORDING TO A NEW STUDY PUBLISHED IN *THE LANCET*, A BRITISH MEDICAL JOURNAL, BY RESEARCHERS AT TEXAS BIOMED AND THEIR COLLABORATORS IN THAILAND.

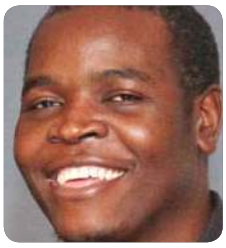
A second study, published concurrently in the journal *Science* by the same research groups, identifies a major region of the malaria parasite genome associated with artemisinin resistance, raising hope that there will soon be effective molecular markers for monitoring the spread of resistance. Both studies were funded by the National Institutes of Health and the Wellcome Trust.

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

Patients infected with malaria parasites who respond poorly to treatment have been observed in Cambodia and stimulated a coordinated World Health Organization effort to eliminate the disease in this region. That effort was based on the premise that drug-resistant malaria was confined to Cambodia. Now that idea needs to be reassessed, *The Lancet* study concludes.

From 2001 until 2010, the Texas Biomed team and their collaborators in Thailand studied 3,202 patients in clinics located in western Thailand, 500 miles from the Cambodian malarial focus area. They observed a dramatic decline in the drug potency over that period. Further, by measuring drug potency in patients infected with genetically identical malaria parasites, they were able to show that the decline in potency results from the spread of resistance genes.





"SPREAD OF DRUG-RESISTANT MALARIA PARASITES WITHIN SOUTHEAST ASIA AND OVERSPILL INTO SUB-SAHARAN AFRICA, WHERE MOST MALARIA DEATHS OCCUR, *would be a public health disaster resulting in millions of deaths.*"

— STANDWELL NKHOMA, PH.D.

"Spread of drug-resistant malaria parasites within Southeast Asia and overspill into sub-Saharan Africa, where most malaria deaths occur, would be a public health disaster resulting in millions of deaths," said Texas Biomed's Standwell Nkhoma, Ph.D., a lead author of *The Lancet* report.

Resistance to other antimalarial drugs, such as chloroquine and fansidar, has previously spread from Southeast Asia to Africa, providing a chilling precedent for such a scenario.

"The problem we have is that treatment with artemisinin-based drugs will promote spread of resistance, but there are no viable alternative treatment options in Southeast Asia," Nkhoma said.

"Our group wanted to understand what genetic changes have occurred in these parasites," said Texas Biomed scientist Ian Cheeseman, Ph.D., the first author of the companion report in *Science*. "This study narrows the search to a region of the parasite genome containing around 10 genes. We haven't yet found the precise changes involved, but we are getting close."

The researchers first compared genetic variants in the genomes of parasites from Laos, which are sensitive to the drug, with parasites from Cambodia, that show high levels of resistance and those from Thailand, where both resistant and sensitive parasites occur.

"We found 33 genome regions that were very different in parasites from these three countries," said Texas Biomed's Tim Anderson, Ph.D. "When we examined these regions in more detail in a large collection of parasites from Thailand, we found that one small section of malaria parasite genome on chromosome 13 is strongly associated with parasite resistance."

Identification of a molecular marker for resistance will be critical for monitoring the spread of resistance, for determining how resistance occurs and for understanding the mechanism of action of the drug. The *Science* study narrows the search for such a marker and provides an important advance in the race to avert a public health crisis.

Both reports were widely publicized in the international news media and resulted from an international effort led by Texas Biomed's Anderson and François Nosten, M.D., at the Shoklo Malaria Research Unit in Thailand, with collaborators at Notre Dame University and in Laos and Cambodia. The other Texas Biomed authors on the reports are Shalini Nair and Salma Al-Saai. ■

Chimpanzees in Biomedical Research at the Crossroads

ALTHOUGH THE INSTITUTE OF MEDICINE (IOM) RECENTLY CONCLUDED THAT CHIMPANZEE RESEARCH IS NECESSARY TO DEVELOP THERAPIES FOR DEVASTATING ILLNESSES NOW AND IN THE FUTURE, THE USE OF CHIMPANZEES IN BIOMEDICAL RESEARCH IS AT A CRITICAL TURNING POINT. JUST WITHIN THE LAST YEAR, SEVERAL DEVELOPMENTS — WHICH ARE BEING CLOSELY TRACKED BY TEXAS BIOMED — COULD JEOPARDIZE THE CONTINUATION OF LIFE-SAVING BIOMEDICAL RESEARCH WITH CHIMPANZEES:

- Prompted by activism from animal rights organizations, the National Institutes of Health (NIH) in 2011 put on hold the scheduled transfer of about 175 chimpanzees from the Alamogordo Primate Facility in New Mexico to Texas Biomed's Southwest National Primate Research Center (SNPRC). The transfer is being delayed even though it would save millions in taxpayer dollars and chimpanzees at the SNPRC would have access to first-rate veterinary care and living conditions.
- Before making a decision on the transfer, NIH requested an assessment by the IOM of the future need for chimpanzees in biomedical and behavioral research. In December, 2011, the IOM issued a report that specified explicit criteria justifying the use of chimpanzees in biomedical research. NIH has established a working group to make recommendations on how to implement the report's findings, and its initial report should be issued soon.
- Despite the NIH/IOM's mandate, proposed legislation called "The Great Ape Protection and Cost Savings Act of 2011" (GAPCSA) is currently before Congress and would end research involving all great apes (e.g., chimpanzees, gorillas, bonobos, and orangutans) by prohibiting federal funding of this research. Ironically, in addition to putting human lives at risk, passage of GAPCSA would actually result in a significant increase in cost to taxpayers.
- In addition, the U.S. Fish and Wildlife Service is considering a petition filed by some of the same animal rights activists which seeks to prohibit chimpanzee research by adding chimpanzees housed in research colonies to the endangered species list.

TAKE ACTION:

Ask your Senators and Representative to **oppose GAPCSA**. Go to:
http://tinyurl.com/cooay2t
to add your name to a letter drafted by the Federation of American Societies for Experimental Biology. Be sure to use the address and zip code where you are registered to vote.

As the IOM recognized, chimpanzee research is of critical importance to human health initiatives. And, according to SNPRC Director John L. VandeBerg, Ph.D., most, if not all, research with chimpanzees at Texas Biomed already satisfies the newly established IOM criteria:

1. There is no other suitable model available, such as in vitro, nonhuman in vivo, or other models, for the research in question.

2. The research in question cannot be performed ethically on human subjects.

3. Forgoing the use of chimpanzees for the research in question will significantly slow or prevent important advancements to prevent, control and/or treat life-threatening or debilitating conditions.

"It is premature to limit chimpanzee research," said Texas Biomed virologist Robert E. Lanford, Ph.D. "Today we do not yet have a hepatitis C virus vaccine, and there are some things on the horizon that will require chimpanzees — such as the very complex process of altering the immune response in people who have autoimmune diseases that are manifested as type I diabetes and rheumatoid arthritis."

The IOM report concluded, "A new, emerging, or reemerging disease or disorder may present challenges to treatment, prevention and/or control that defy non-chimpanzee models and available technologies and therefore may require the future use of chimpanzees." VandeBerg characterized chimpanzees housed in biomedical research institutions as an invaluable research resource that could be essential to combat deadly new infections.

"As a consequence of the IOM report, the chimpanzee is still available for tests where it is the only animal we can use to achieve our important goal in advancement of medicine," said Thomas Folks, Ph.D., SNPRC's director of research resources. "But a major concern now is whether attempts will be made to limit research with other species."

Texas Biomed and its representatives continue to track these developments and are working closely with other scientific organizations to defeat GAPCSA and other efforts to ban crucial biomedical research with chimpanzees. Texas Biomed will follow the developments described above and seek additional support if warranted.

Several highly respected scientific organizations have posted a legislative action alert urging their members to write to Congress in opposition to GAPCSA. Any interested party can write to their elected officials through the link in the box on page 8.

In addition, testimony before the Senate Subcommittee on Water and Wildlife on GAPCSA from James Anderson, Ph.D., who oversees the chimpanzee research program for the National Institutes of Health, is at:

http://tinyurl.com/cej5y6o

A recent response from directors of primate centers that house chimpanzees to the comments of Rep. Roscoe Bartlett, an original sponsor of the GAPCSA, that appeared in The Hill newspaper is available at:

http://tinyurl.com/bmqvnl3

NEED FOR CHIMPANZEE RESEARCH:

1. Better treatments for hepatitis B and C.
2. Vaccine for hepatitis C.
3. Therapies for new, emerging, or reemerging diseases and disorders.
4. Development of new monoclonal antibodies aimed at treating cancers and autoimmune diseases.
5. Behavioral studies.

ADVANCES DUE TO CHIMPANZEE RESEARCH:

1. Development of vaccines for hepatitis A and hepatitis B — now given to children in 116 countries.
2. Finding that dietary salt is a major causative factor of elevated blood pressure.
3. Development of FDA-approved monoclonal antibodies for use in treating lymphomas and other cancers.
4. Testing of potential and currently marketed "wonder drugs" such as monoclonal antibodies for treating autoimmune disorders.
5. Development of the polio vaccine.

New Animal Model May Lead to Treatments for a Common Liver Disease Which Affects Millions of Americans

Scientists at Texas Biomed have developed the laboratory opossum as a new animal model to study the most common liver disease in the nation — afflicting up to 15 million Americans — and for which there is no cure.

The condition, nonalcoholic steatohepatitis (NASH), resembles alcoholic liver disease, but occurs in people who drink little or no alcohol. The major feature of NASH is accumulation of fat in the liver, along with inflammation and functional damage. Most people with NASH feel well and are not aware that they have a liver problem. Nevertheless, NASH can progress to cirrhosis, in which the liver is permanently damaged and no longer able to work properly. NASH-related cirrhosis is the fourth most common indication for liver transplantation in the U.S.

NASH affects 2 to 5 percent of Americans — roughly six million to 15 million people. An additional 15 to 30 percent of Americans have excess fat in their livers, but no inflammation or liver damage, a condition called "fatty liver" or the non-progressive form of nonalcoholic fatty liver disease (NAFLD).

The study, published in the July issue of the *American Journal of Physiology-Gastrointestinal and Liver Physiology*, was supported by the National Institutes of Health and the Robert J. Kleberg, Jr., and Helen C. Kleberg Foundation.

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

Both NASH and NAFLD are becoming more common, possibly because of the greater number of Americans with obesity and its important health complications, type 2 diabetes, high blood cholesterol levels, high blood pressure and other risk factors for heart attack and stroke. In the past 10 years, the prevalence of obesity has doubled in adults and tripled in children. It was previously reported by other scientists that the prevalence of NAFLD and NASH in a cohort of middle-aged patients in San Antonio is 46 percent and 12 percent, respectively.

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

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

Development of Animal Model and Drug Tests Show Advances Against Deadly Viruses

SCIENTISTS AT TEXAS BIOMED HAVE RECENTLY DISCOVERED A NEW ANIMAL MODEL AND TWO OFF-THE-SHELF DRUGS THAT MAY HELP IN THE FIGHT AGAINST DEADLY VIRUSES THAT ARE POTENTIAL BIOTERRORISM WEAPONS AND WHICH HAVE NO TREATMENTS OR VACCINES.

A study published in the journal *Virology* reports that the common marmoset, a nonhuman primate, is susceptible to experimental infection with a family of deadly viruses, including Ebola and Marburg.

Ebola and Marburg infection can be acquired through infected persons, animals and in laboratory settings. These infections cause hemorrhagic fever, which begins with flu-like symptoms and progresses rapidly to the final stages characterized by fever, bleeding, and severe low blood pressure that is fatal in 90 percent of cases. No drug has been approved to treat infection by either virus. People diagnosed with Ebola or Marburg currently only receive supportive care and treatment for complications.

MARMOSETS ARE BETTER MODELS THAN OTHER NONHUMAN PRIMATES

Nonhuman primates are good models to study infectious disease because their immune system is similar to humans and they are good predictors of vaccine efficiency. The marmoset is a better model than other nonhuman primates such as macaques, which are more risky for transmitting certain diseases to humans and generally more difficult to handle.

"The common marmoset is a smaller, and easier-to-use model in which the animal can be tested earlier in the disease process in order to develop a vaccine," said Ricardo Carrion, Ph.D., a Texas Biomed virologist.

The report, with Texas Biomed scientist Jean L. Patterson, Ph.D., as co-author, was funded by the National Institutes of Health (NIH) and the Texas Biomedical Forum. The study was made possible using Texas Biomed's biosafety level 4 maximum-containment laboratory.

NEW ANIMAL MODEL:

Researchers at Texas Biomed discovered that the common marmoset is susceptible to experimental infection with a family of deadly viruses, including Ebola and Marburg. Marmosets are good models because their immune system is similar to humans. Also, they are a better model than other nonhuman primates because they are smaller and generally less difficult to handle.

The researchers found that inoculation with small amounts of Ebola virus and Marburg virus caused conditions in the marmoset similar to those observed in human disease. Most notably, animals experienced reduced blood platelet levels, a high number of white blood cells indicating infection, and clotting interrupting normal blood flow to body organs — all of which occur in humans afflicted with these diseases.

"Texas Biomed is working with the NIH and Defense Department to have a vaccine available for human clinical studies by 2015," said Patterson. "We believe that the marmoset is a great model."

The increased frequency of outbreaks of hemorrhagic fever caused by Ebola and Marburg in central and western Africa and the potential use of such agents as biological weapons underscore the need to understand pathogenesis of these viruses and to develop effective intervention strategies. These viruses have also been responsible for an 88 percent decline in chimpanzee populations since 2003.

TWO CANCER DRUGS BLOCK EBOLA VIRUS

In another development, Carrion and his colleagues found that two off-the-shelf cancer drugs blocked the Ebola virus from reproducing in the test tube. The finding is an early and promising advance. Testing of the drugs took place in Texas Biomed's biosafety level-4 laboratory in collaboration with government scientists and researchers in Houston and Atlanta.

The two leukemia drugs, nilotinib and imatinib, don't attack the virus directly, but instead target the patient's own infected cells, preventing the virus inside from reproducing and escaping. The approach is attractive because scientists can target a cellular protein that is required for the virus, making it more difficult for the virus to mutate and develop resistance. The study was led by Gary Nabel, M.D., Ph.D., director of the vaccine research center at the National Institute of Allergy and Infectious Diseases (NIAID), and published in the journal *Science Translational Medicine*. The work was funded by NIAID, a division of the NIH.

While the drugs didn't completely clear the virus, researchers say that outbreaks of disease in Africa show that those with low levels of the virus in their bodies often survive. The hope would be that a short-term course of treatment with the drug might eliminate enough of the virus so that the patient's own immune system could eliminate the rest.

The next step is to test it in animals. Because Ebola outbreaks in nature are so infrequent and unpredictable, it makes human testing almost impossible, researchers say. It appears sporadically in a handful of African nations.

"We're still trying to identify the reservoir," said Carrion. "We don't even know what maintains it in nature." ■

BOARD OF TRUSTEES

TEXAS BIOMEDICAL RESEARCH INSTITUTE

PROGRESS

Progress is a publication of the Texas Biomedical Research Institute. If you would like to be added to our mailing list or to update your mailing information, please contact Joseph Carey at **jcarey@TxBiomed.org**

Editor: Joseph Carey, Vice President for Public Affairs
Design and production: Ideawire
Photography: Larry Walther

TEXAS BIOMEDICAL
RESEARCH INSTITUTE
PO Box 760549
San Antonio, TX 78245

CAMPUS BRIEFS

High School Science Teachers Visit Campus

On June 28, Texas Biomed hosted a day on the campus for 18 San Antonio area high school science teachers. Jerilyn Pecotte, Ph.D. (second row, second from the right) organized the day's events, which included a welcome from Texas Biomed President Kenneth P. Trevett and a briefing and campus tours by Vice President for Institutional Advancement Corbett Christie (second row, first on the left). Tours included visits to the Southwest National Primate Research Center animal colonies and the AT&T Genomics Computing Center. Laboratory tours and presentations were given by Joanne Curran, Ph.D., Anthony Griffiths, Ph.D., Hareesh Nair, Ph.D., Matthew Johnson, Ph.D., Kimberly Spradling, Ph.D., Heath Nevill and Bob Baker, D.V.M.

Texas Biomed Receives Funding to Test Vaccines Against Deadly Viruses

Texas Biomed scientists have recently been awarded $3.6 million from the Defense Department and the National Institutes of Health to characterize and test vaccines against several filoviruses, some of the world's most deadly viruses. Ebola and Marburg are highly lethal hemorrhagic fever viruses with fatality rates up to 90 percent and are potential bioterrorism weapons. Because of these threats, there is a pressing need for effective vaccines and treatments for these viruses.

In one project, Anthony Griffiths, Ph.D., with other laboratories in the Department of Virology, is characterizing filoviruses to be used in vaccine and antiviral studies, as well as developing and refining tests to determine the effectiveness of filovirus vaccines and therapies.

In addition, Ricardo Carrion, Ph.D., and Jean Patterson, Ph.D., are working with the Lovelace Respiratory Research Institute in New Mexico to test in monkeys the efficacy of candidate filovirus vaccines, using Texas Biomed's biosafety level 4 laboratory. They will also perform immunological tests during the research to gain a better understanding of the immune responses elicited by different vaccine candidates under differing schedules or conditions. ■