# PROGRESS

# Spring 2019

#### **Surviving a Superbug** Rex and Deborah Amini



# Texas Biomed and UT Health Team Up to House Geriatric Marmosets

exas Biomed uses its population of approximately 340 marmosets for various research projects, including experiments involving the emerging Zika virus and research into Parkinson's disease. The marmosets from UT Health San Antonio's Barshop Institute are used in aging research as part of the San Antonio Marmoset Aging Program (MAP). Combined, these programs will maintain more than 400 marmosets for research, making it the country's largest marmoset colony dedicated to aging and infectious diseases research.

Marmosets are small New World monkeys that are excellent animal models in many areas of biomedical research.

"Marmosets are becoming an increasingly important biomedical model and are of particular interest in aging studies, due to their relatively short life span compared with other types of primates. The SNPRC has dedicated facilities and staff for the care and management of this unique species," said Professor Suzette Tardif, Ph.D., Associate Director of the SNPRC.

Texas Biomed recently invested more than \$2 million updating an entire building devoted to the care of this species with the capacity to hold up to 550 marmosets.

"To understand aging and how interventions such as exercise, diet and pharmacological agents might improve health across the life span, it is helpful to conduct comparative biology studies across species, including rodents and small animals. Marmosets have proven to be a great addition to the science of aging," said Nicolas Musi, M.D., Barshop Institute Director and Professor of Medicine in the Joe R. and Teresa Lozano Long School of Medicine at UT Health San Antonio.

The MAP colony of marmosets at Texas Biomed will be made up of 90 to 175 animals including a population of geriatric marmosets (animals between the ages of 10 and 20 years old) and a population of mid-life marmosets



The Common Marmoset photo by Kathy West Studios.

(between 6 to 9 years old) necessary for future aging studies.

Prior to their transport to Texas Biomed from the Barshop Institute, marmosets will undergo a medical evaluation to make

sure they are healthy enough to move. Once the animals are housed at Texas Biomed, their care will be overseen by SNPRC staff and the Institutional Animal Care and Use Committee (IACUC) on the Texas Biomed campus.

"The agreement between UT Health San Antonio and Texas Biomed to jointly manage the Marmoset Aging Program, housed at Texas Biomed, is an example of the highly collaborative relationships between our biomedical science institutions in San Antonio," said Professor Joanne Turner, Ph.D., Texas Biomed VP for Research. "We see ourselves as collaborators and not competitors within the biomedical science space, and Texas Biomed welcomes additional citywide interactive projects in the future."

Texas Biomed and UT Health are both engaged in research and public health missions. This collaboration is a reflection of those shared values.

"The National Institutes of Health plans to launch funding to expand marmoset research, and this agreement will provide an exceptional resource to our institutions and collaborators to understand the neurobiology of aging and treat conditions ranging from neurodevelopmental and neurodegenerative disorders to infectious diseases," said Professor Andrea Giuffrida, Ph.D., Vice President for Research at UT Health San Antonio.

The agreement to merge these research animals to one location at the SNPRC was signed earlier this month. The animals will be transferred this summer.

# Searching for Protection for HIV Patients from Deadly Tuberculosis

ne third of all HIV/AIDS patients die of complications from TB. The same mechanism of HIV/AIDS that leads to the loss of immune cells (CD4+ T cells) in other parts of the body also targets the lungs, opening the door for a latent infection with *Mycobacterium tuberculosis (Mtb)* bacteria to become active TB.

Director of the Southwest National Primate Research Center Professor Deepak Kaushal, Ph.D. says research he collaborated on is pinpointing a possible new avenue of protection for HIV/AIDS patients. The study, published in the journal Cell Reports helps scientists better understand how HIV promotes deadly cases of tuberculosis (TB).

"If our findings are validated in future testing, this will lead to the potential for new therapies (including perhaps host-directed) that would prevent the loss of these crucial T cells during HIV infection," Dr. Kaushal said. "The idea is that fewer HIV patients would progress to TB."

Until now, scientists weren't too sure which parts of the lungs were targeted by the immunodeficiency. Dr. Kaushal conducted his work on rhesus monkeys infected with TB and SIV (simian immunodeficiency virus). Collaborators at Brigham and Women's Hospital in Boston, Massachusetts, led by Dr. Bjorn Corleis, collected tissue either from a humanized mouse model or from humans. What both groups found was that not all T cells in the lungs are affected by HIV — only the ones embedded inside the lung tissue. T cells in the lung sacs (alveoli) where oxygen enters the blood stream were still functional.

This information is "important to know because we can target vaccines, therapeutics and drugs to these specific T cells in the lungs," Dr. Kaushal explained.

Around the globe, the number of AIDS-related deaths is more than a million people annually. Since the beginning of the epidemic 35 years ago, more than 39 million people have died from the infectious disease.



Mycobacterium tuberculosis bacteria. Photo courtesy: NIH Image Gallery

Co-infections with HIV and TB are a persistent health problem. In otherwise healthy people with latent TB, only 5% will go on to develop active tuberculosis. In HIV/AIDS patients, the risk of developing active TB increases tenfold to 50%.

This research was funded in part by grants from the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of General Medical Sciences (NIGMS), and the National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH). Other financial support was provided by the Burroughs Wellcome Fund.

Collaborators on the paper include researchers from Ragon Institute, Massachusetts General Hospital, Harvard Medical School, Tulane University School of Medicine, Tulane National Primate Research Center, Southwest National Primate Research Center, and Washington University School of Medicine.

"I do anticipate that we will get to the top of HIV and TB in the next 50 years," Dr. Kaushal said. "This is an exciting time to be in this research area."

#### **Surviving a Superbug**

#### Rex and Deborah Amini

The quintessential Texan, Rex Amini carries himself with authority. His wife, Deborah, describes him best, "He has always been this larger than life person, stronger than anyone I have ever known. He has this tough veneer, but I know it is just a veneer."

A family man, Rex has three children. He runs an oil business with his brothers, spends time with Deborah on a variety of charities focused on inner-city education initiatives, and is a self-described outdoorsman. His collection of archaeological gems, global artifacts and hunting trophies are small glimpses into his impressive life story.

But, for 84 days beginning in November 2018, Rex was at the mercy of tiny bacteria that colonized in his cervical spine. Diagnosed with Methicillin-resistant Staphylococcus aureus (MRSA), he and his family and friends agonized, prayed and battled alongside a team of doctors for Rex's future.

Racked with chills and fever, Rex thought he had the flu. His doctor miraculously had the foresight to perform a blood culture. Rex was rushed to the emergency room for MRSA treatment, where an infectious disease physician and a neurosurgeon collaborated on a treatment plan that not only saved Rex's life but managed to ensure he would walk again. The bacteria were putting pressure on his spinal cord, which could have caused permanent paralysis. An emergency surgery relieved pressure from the bacteria buildup to lessen the danger of paralysis, but it took two weeks to find the appropriate cocktail of drugs to fight the infection.

Rex doesn't recall most of the month of December. In addition to fighting the bacteria, his body was so weakened from the infection, he went into pulmonary failure twice. His incredible recovery now consists of physical therapy appointments to strengthen his right side in the hopes of returning to his golf game soon.

"When something like this happens that is so much greater than anything you have ever known, it is an ever-present reminder that we really control nothing," Deborah explained. "Our community, with places like Texas Biomed, the hospitals, the family and friends, the financial means we have is a reminder that we are blessed and called to do something for people who don't have these resources."

Deborah recalled the numerous rooms and patients the infectious disease physician visited during the time Rex was in the hospital, and she was in awe of the scope of the infectious disease problem.

"Here's the bottom line," Rex said. "These bugs are becoming resistant to the current means we have to control them, and this is becoming a bigger and bigger problem. There are scientists who say if you think cancer and heart disease are problems to the health of Americans, just wait until these superbugs become completely resistant to treatments. This problem is global, and we are obligated to look beyond the borders of our own country."

Rex believes in the power of science, and happens to be a member of the Texas Biomed Board of Trustees. He joined the board several years ago simply because of a love of science. But, his latest health journey has provided him an even greater sense of purpose and appreciation for the power of science. Rex and Deborah shared that their good fortune and miracles were a direct result of access to treatment and medication.

"These antibiotic cocktails that saved my life are a direct result of science," Rex said. "What the infectious disease doctor was doing clinically was based on the science being done by researchers like those at Texas Biomed. He is standing on their shoulders."



Rex Amini. Photo above and cover photo by Josh Huskin.

# Another Piece of the Ebola Puzzle Identified

A team of researchers have discovered the interaction between an Ebola virus protein and a protein in human cells may be an important key to unlocking the pathway of replication of the killer disease in human hosts. Scientists at Texas Biomedical Research Institute were part of a nationwide collaborative with scientists at Gladstone Institutes, UC San Francisco and Georgia State University for a study recently published in the journal *Cell*.



Ebola virus (red) replicates much faster in human macrophages depleted of RBBP6 protein (right panel). Photo Courtesy of Dr. Olena Shtanko

Scientists around the globe are trying to pinpoint potential drug targets to stop Ebola virus disease, a hemorrhagic fever that killed 382

people in the latest outbreak in the Democratic Republic of Congo in 2018. Thousands of people have died from Ebola since an outbreak erupted in West Africa four years ago.

Staff Scientist Olena Shtanko, Ph.D., describes this new work as a "turning point for understanding how replication of Ebola virus is modulated." Her role in the project was to validate and test whether the interaction between an Ebola virus protein called VP 30 and a host (human) protein called RBBP6 had involvement in the life cycle of the virus. Dr. Shtanko worked on this project while in the lab of Dr. Robert Davey, a former Texas Biomed Scientist, now at Boston University.

Earlier research by scientists in California used a protein interaction map to narrow down host and virus protein interactions and then using a yeast system and an artificial proxy virus system proved the theory of this particular protein-protein interaction. However, scientists needed to use replicating virus and human immune cells to test the clinical significance of the finding.

"The interaction is important if you can show functional significance of what it does to the virus in cells that have clinical relevance," Dr. Shtanko stressed. "If you can figure out the mechanism within these cells, then you can potentially manipulate it and stop the disease progression."

Staff Scientist Eusondia Arnett, Ph.D., and President and CEO Dr. Larry Schlesinger – both tuberculosis researchers – have expertise in working with human macrophage (immune) cells drawn from donated blood samples. "We were able to capitalize on our experience with macrophages to over-and under-express the RBBP6 (host) protein to create an effective model for this important Ebola virus research," Dr. Arnett said.

By over- and under-expressing the RBBP6, Dr. Shtanko was able to test what impact the protein had on the growth of Ebola virus in the macrophages. Dr. Shtanko said the results were striking. When the host protein was under-expressed, the viral replication went up exponentially. She found similar results when working with vascular cells, which are also key to Ebola virus replication in an infected patient.

The study was also an example of the Institute's new team science environment; whereby, researchers capitalize not only on the resources available at Texas Biomed but the expertise of its cross-functional teams (i.e. Ebola virus and macrophage biology) to produce beneficial results.



Staff Scientist Olena Shtanko, Ph.D.



P.O. Box 760549 San Antonio, TX 78245



#### A Note from the President/CEO Texas Biomed's focus is on you

S cience involves data collection, experimentation, equipment and highly-educated personnel. These components of research are not our focus at Texas Biomed, though. You are the focus — you, your family, and our global community.

In an effort to pave the way to a healthier world, our projects run the gamut from studying viruses and bacteria that cause scourges like HIV, Ebola, and malaria, to causes of drug resistance, new approaches to treatments and vaccines and pinpointing genetic components contributing to common health problems like obesity and diabetes, which put people at higher risk for infection.

Sharing our science is part of our important mission to pioneer scientific breakthroughs that protect the world from the threat of infectious diseases, particularly those most vulnerable. With our mission in mind, we've updated our scientific programs and are recruiting toptier researchers to achieve our goal of becoming the leader in infectious disease research.

In this issue of *Progress* magazine, you'll read about some of our recently published journal articles. These are results of our scientific studies deemed so important, they've been distributed by some of the most highly-regarded publications in the field to inform others about our scientists' successes.

For donor Rex Amini and his wife Deborah, science gave them a future. His story is a perfect example of why so many of our ardent supporters believe in what we're doing.



Larry S. Schlesinger, M.D.

People like the Aminis are passionate in their support of our mission, and we are truly grateful. Our nonprofit business model could not work without them.

Thank you for taking the time to peruse these pages and learn more about the incredible breakthroughs that are taking place in San Antonio, and ultimately, impacting people all over the world.

Jobl