





## The San Antonio Partnership for Precision Therapeutics



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## The San Antonio Story



## **Presidents' Message**

Innovation, ingenuity and progress require bold thinking. Meaningful change requires action. As the leaders of four prominent San Antonio research institutions, we are taking action and combining resources to create an aggressive, new health care approach. Building upon the critical research that has been happening in San Antonio for decades, we envision personal, precise patient care and drug therapy with a global reach, and our collaboration as the vehicle to get there.

Independently, our organizations maintain world-class resources, provide exceptional patient care and employ thousands of health care professionals and scientists conducting cutting-edge research and making significant breakthroughs. Together, we are stronger. Together, we broaden our impact.

In 2019, Southwest Research Institute, Texas Biomedical Research Institute, The University of Texas at San Antonio and UT Health San Antonio united to form the San Antonio Partnership for Precision Therapeutics (SAPPT). With the commitment of San Antonio Mayor Ron Nirenberg, city and business leaders, and scientific and technical committees, we launched the SAPPT to advance the science of precision therapeutics by leveraging each of our institution's unique strengths and fostering the robust bioscience ecosystem in our region.

Together, our preeminent organizations possess vast resources and professional networks to carry an innovative idea from the lab to the community. By building on our rich history of collaboration and sharing technology, facilities, and expertise, we can truly transform lives. Through the SAPPT, we have canvased our resources and are collectively addressing bioscience challenges to advance precision patient care and treatment.

After just over a year of partnership, we have established an efficient infrastructure, supporting five active projects, all with the potential to revolutionize health care. In the years to come, we look forward to advancing the impact and reach of the SAPPT, while strengthening San Antonio as a bioscience hub. Here, smart collaboration - based in innovation - will certainly thrive and change the world.



#### Larry Schlesinger, M.D.

Texas Biomedical Research Institute President & CEO

#### William L. Henrich , M.D., MACP

UT Health San Antonio President

#### Taylor Eighmy, Ph.D.

The University of Texas at San Antonio President

#### Adam L. Hamilton, P.E.

Southwest Research Institute President & CEO

## Message from Mayor Ron Nirenberg



San Antonio, Texas is at the intersection of all things: history and progress, the military and business, culture and inclusion. Physically, our city is at the intersection of commerce in the United States, where Interstate 35 connects the north and south, and Interstate 10 connects the east and west. At the heart of our medical community is the intersection of innovation and compassion, embodied by our robust and people-driven biosciences industry.

We're the 7th largest city in the U.S., but across our three-century history, we've maintained our character as one of the country's great and unique cities. Along the way, with the support of organizations such as the San Antonio Economic Development Foundation, San Antonio built a community supportive of fostering and promoting medical innovation, research and development.

Here, medicine is at the intersection of the private, nonprofit, academic and government sectors with organizations such as the Southwest Research Institute, Texas Biomedical Research Institute, UT Health San Antonio and The University of Texas at San Antonio. The presidents of these organizations came together to form the San Antonio Partnership for Precision Therapeutics — a truly game-changing commitment to collaborative, personalized therapies to treat chronic disease.

And it's rare to describe San Antonio without mention of the military. We're home to Joint Base San Antonio, the Army Medical Command, Air Force's 59th Medical Wing, The Navy Medicine Education and Training Command, Brooke Army Medical Center, and the Center for the Intrepid — institutions that conduct important medical research , including the U.S. Institute of Surgical Research where the military's only burn unit resides and cutting-edge burn therapies for service members and civilians alike are continually under development and improved upon every day.

Amid the global coronavirus pandemic , institutions across San Antonio lead the way in COVID -19 research as our Health Transition Team has provided imperative guidance on how our community could safely implement the staged reopening of our local economy.

Our diverse medical and bioscience community has come together to form an ecosystem that's cooperative and supportive — one that drives innovation to improve lives — and that's attractive to startups, legacy corporations, and top talent. We are committed to the industry and excited about its future because it is one with our own.

**Mayor Ron Nirenberg** 



Texas Biomed is where health starts, delivering both independent and collaborative research that has translated into new discoveries, therapies and vaccines to fight diseases such as AIDS, COVID-19, Ebola, hepatitis, tuberculosis, parasitic diseases and chronic conditions related to infection and inflammation like diabetes and heart disease.

R&D Hot Spot

IN FEDERAL R&D EXPENDITURES



## **The San Antonio** Advantage





UNMATCHED COLLABORATION BETWEEN MILITARY AND PRIVATE SECTOR



☆

For more than 300 years, San Antonio has been a center of discovery, exploration and partnership, attracting innovators and enterprise from across the globe. San Antonio's cultural roots and intellectual diversity run deep, and the region enjoys a long history of partnership among health care, academic, research and development, technology and military communities.

Lots of places claim a "small town feel" but few can back it up with big city opportunity. The ultimate San Antonio advantage is found in the genuine support, authentic camaraderie and sincere enthusiasm for one another's successes.



San Antonio jobs grew by 9.5%, outpacing the national growth rate of 6.2% (2015-2020)

NO N

Photo courtesy of San Antonio **Economic Development Foundation** 

**High-Quality Affordability** 



## \$325+ MILLION AWARDED TO SAN ANTONIO'S MAJOR BIOMEDICAL RESEARCH INSTITUTIONS THAT COMPRISE THE SAPPT

## 1 OUT OF 6 SAN ANTONIANS WORK IN BIOSCIENCE & HEALTH CARE



## MORE THAN 39,000 MILITARY TRAINING GRADUATES COME THROUGH S.A. ANNUALLY



## LARGEST U.S. INSTALLATION



LARGEST DEPARTMENT OF DEFENSE MEDICAL CENTER







# **San Antonio** Partnership for Precision Therapeutics



## **Precision Therapeutics**

Precision therapeutics offers patient-focused, personalized health care solutions through targeted research, notable drug discovery and more effective interventions and therapies. This is not the standard, one-size-fits-all medicine, but rather a tailored, personalized approach to medicine based on a patient's individual lifestyle, environment and biology that is backed by research on specific populations.

Precision medicine generally focuses on personalized interventions based on genetics, environment and diet. Precision therapeutics merges this discipline with a complete drug discovery pathway, integrating the two in a way that has never been done before.

## **Partner Institutions**

Driven by a shared vision to leverage the robust scientific community and strengths of one of the fastest growing cities in America, the leaders of four prominent research entities united in a groundbreaking collaboration. In 2019, a powerful partnership was formed to align the unparalleled bioscience capabilities, resources and military medicine opportunities in San Antonio to improve health care in Texas and beyond.

Together, Southwest Research Institute (SwRI), Texas Biomedical Research Institute (Texas Biomed), UT Health San Antonio and The University of Texas at San Antonio (UTSA) advance innovative and high-impact biomedical research in precision therapeutics. One of the main goals of the collaboration is to accelerate getting therapies and pharmaceuticals from basic research to people in need.

To improve health care in Texas and beyond, SwRI, Texas Biomed, UT Health San Antonio and UTSA each contribute unique assets and expertise to the SAPPT.

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#### **Southwest Research Institute**

Southwest Research Institute is one of the oldest and largest independent, nonprofit, applied research and development organizations in the nation. With nine technical divisions, SwRI engineers and scientists create innovative solutions for a range of challenges, from Deep Sea to Deep Space<sup>®</sup>. SwRI has a rich history of advancing patient care through the development of pharmaceuticals, bioengineered materials, and drug delivery systems. The organization has licensed multiple technologies to fight infectious disease, reduce pain and treat addiction, mitochondrial poisoning and cancer. SwRI offers vast expertise in micro and nanoencapsulation technologies that solve challenging drug delivery problems and accelerate drug discovery and development. SwRI maintains FDA-inspected and Current Good Manufacturing Practice (CGMP)-certified facilities where it conducts pharmaceutical development and complex synthesis and formulation of quality products for preclinical and clinical testing. SwRI is committed to advancing bioscience to benefit government, industry, and all of humanity.

#### **Texas Biomedical Research Institute**

Since its founding in 1941, Texas Biomed has gained worldwide recognition for the quality of its basic research. The Institute is a global leader in the science of infectious diseases and their associations with other disease states and susceptible populations. The organization's strengths include research programs in tuberculosis, HIV, malaria, hepatitis and hemorrhagic viruses, aging and complex metabolic disorders. The Institute is home to three interdisciplinary scientific programs (Host-Pathogen Interactions, Disease Intervention and Prevention, and Population Health) and is the only place with both a National Primate Research Center and a privately-owned biosafety level four maximum containment laboratory. By conducting research that leads to breakthrough discoveries and sharing what we learn, we are leading the fight to reduce unnecessary anxiety, suffering and death due to infection. Our hope is a healthier world free from the reality of infectious disease.

#### **UT Health San Antonio**

UT Health San Antonio is a public university within the University of Texas System and serves as the region's only academic Health Center. UT Health San Antonio offers over 70 degree specialties across its five schools of medicine, nursing, dentistry, health professions, and graduate biomedical sciences. UT Health San Antonio, one of the nation's leading biomedical research institutions, is home to the Mays Cancer Center, a clinical and research enterprise affiliated with the world-renowned MD Anderson Cancer Center and one of only four National Cancer Institute Designated Cancer Centers in Texas, which is also home to the renowned Institute for Drug Development. UT Health San Antonio also features the Center for Renal Precision Medicine, the Center on Smart and Connected Healthcare Technologies, the Biggs Institute for Alzheimer's and Neurodegenerative Diseases, and the Barshop Institute for Longevity and Aging Studies.

#### The University of Texas at San Antonio

UTSA is dedicated to the advancement of knowledge through research and discovery, teaching and learning, community engagement and public service. The University's research portfolio is heavily focused on biomedicine, including neuroscience and brain health, infectious diseases, and regenerative and molecular medicine. Additionally, it is home to the nation's top cybersecurity program and has robust expertise in cloud computing, data analytics and artificial intelligence, which will lead to technological innovation and the creation of new algorithms to accelerate drug discovery and therapeutics. Its Center for Innovative Drug Discovery, a joint venture with UT Health San Antonio, provides core facilities and expertise to facilitate the translation of basic scientific discoveries into tangible pre-clinical candidate drugs that can be further developed into clinical therapies for human disease.

Southwest Research Institute scientists support in its world-class, FDA-inspected CGMP facilities.



## **Action Model**

The SAPPT uniquely leverages its partner assets and expertise to create a competitive advantage for San Antonio and elevate the biosciences ecosystem to the international stage. Through this partnership, San Antonio is positioned to revolutionize the development and delivery of therapeutics in a holistic way. This collaborative model could define health care around the world for generations to come.

#### The model achieves the following:

- Serves as a novel generator for advanced and timelier biomedical breakthroughs that accelerate the delivery of life-saving treatment options.
- Aligns and maximizes the unique research and service delivery capabilities of each of the participating institutions.
- Promotes the integration of basic research and therapeutics channels with innovative "multi-omic" or big data integration of precision medicine with the goal of developing novel precision therapies and/or approaches to individualized therapies in any disease area.

SAPPT merges the resources of stellar academic and research institutions to integrate the complete drug development pathway from basic research, drug discovery and testing to clinical trials, to more effective life-saving solutions. New discovery is driven by maximizing emerging technology and scientific data.

- Deepening understanding of human biology for diverse populations
- Bold new approaches to resistant diseases
- Drive down the cost of care
- Improve the lives of patients

By overlaying the research and therapeutics channels with innovative big data integration in precision medicine, this partnership provides the infrastructure to develop individualized therapies in an effort to address the specific and diverse medical needs of San Antonio's growing population.



## **Key Projects**

The San Antonio Partnership for Precision Therapeutics has merged the resources of stellar academic and research institutions to integrate the complete drug development pathway from basic research, drug discovery and testing to clinical trials, to more effective life-saving solutions.

The organization aims to lead by example and prioritize efficacy. Through true collaboration and with a shared commitment to efficiency, the SAPPT cycle time from RFP to active project status is only two to four months. With two publications in development, SAPPT is leading by example and shifting the paradigm of how new treatments are developed.

In its first year, the SAPPT facilitated more than \$1 million of investment in five active projects, whose research teams included all four partner institutions and involve more than 35 researchers. Four of the five active projects target COVID-19, with applications to other diseases and viruses.

The combined network of institutional labs and research teams are uniquely positioned to lead global COVID-19 intervention efforts. San Antonio's position on the front lines of developing vaccines and treatments for COVID-19 is supported by critical support from organizations such as USAA and the USAA Foundation, which donated \$1 million for COVID-19 medical research and equipment. Contributions such as that of USAA propel collaborative research efforts that will ultimately result in new, more effective therapies for San Antonio and beyond.

#### MULTI-ORGAN FAILURE DUE TO SEPSIS

The objective of this 5-scientist research team is to identify why some patients are more likely to die from sepsis and to develop a treatment that reduces organ dysfunction and damage after a sepsis diagnosis. An estimated 30 million people worldwide are affected by sepsis every year, and each patient reacts in a distinct manner. While some require antibiotics only, others may require combination therapies to recover. By administering multiple treatments at once, a sepsis patient may have a better chance of surviving and restoring organ function.

The research team is examining the mitochondrial calcium uniporter (MCU) channel that carries calcium to cells. In some sepsis patients, an overflow of calcium floods the channel, bombarding and killing healthy cells, causing organ failure. The team aims to develop a drug therapy that controls the flow of calcium through the channel, allowing only necessary amounts of the element to reach cells.

#### **COVID-19 VACCINE**

This 12-scientist research team is led by microbiologist Dr. Karl Klose, director of the South Texas Center for Emerging Infectious Diseases (STCEID) and professor of microbiology at UTSA. Dr. Klose's team is developing a novel vaccine to combat COVID-19 based on decades of work on a vaccine to combat the bio-weapon, tularemia. Also known as "rabbit fever," tularemia is an infectious disease caused by the bacterium Francisella tularensis. An advanced tularemia vaccine candidate has been developed at UTSA, and the collaborative team isusing this vaccine as a platform to develop a protective COVID-19 vaccine. The team is leveraging their expertise in vaccine development, virology, bacterial genetics, immunology, and chemical formulation. The critical target for immunity against COVID-19 is the spike protein of the SARS-CoV-2 virus, which allows the virus to enter cells and cause disease. The team is testing various forms of the SARS-CoV-2 spike protein that have been expressed in the tularemia vaccine for their ability to protect against COVID-19. The supporting team assembled from the four research institutions brings decades of expertise in their respective fields: Dr. Kenneth Carson, SwRI; Dr. Peter Dube, UT Health San Antonio; Dr. Luis Giavedoni, Texas Biomed.

#### HOW SARS-COV-2 EVADES INNATE IMMUNITY

The ultimate goal of this 8-person team's research is to better understand how the SARS-CoV-2 virus evades our innate immune system and to use that knowledge for the development of new treatments. Targeted destruction of key immune proteins is a common strategy that viruses use to evade our immune defenses. The Orf10 protein of SARS-CoV-2 is thought to be responsible for this activity, but its targets in our immune system remain unknown.

The research team is working to identify human proteins targeted by Orf10 and to discover small molecules that block Orf10's ability to degrade our immune defenses. Unique reagents have been generated to identify Orf10 targets, and the team is using mass-spectrometry approaches to accomplish this goal. The development of a high-throughput assay will be used to discover Orf10 inhibitors in large chemical libraries. With a better understanding of how Orf10 selectively destroys human proteins, the team could harness this activity to selectively destroy pathogenic proteins, such as those responsible for cancer development and progression.

#### **RNA MODIFICATION BY COVID-19**

Dr. Yogesh Gupta of UT Health San Antonio is leading a 6-person team to studying how the novel coronavirus evades the human immune system, by mimicking the host RNA and growing inside the body. RNA is present in all living cells with the principal role of acting as a messenger for controlling the synthesis of proteins. For survival of the virus, its RNA must be protected from degradation inside host cell. COVID-19 produces some proteins that modified its RNA, allowing it to act as a camouflage inside the human body.

By understanding this process, the goal is to develop novel inhibitors that can block specific pathways that permit the virus to replicate inside the host cell. The innovative drug discovery platform will pave the way in developing a new class of drugs to fight COVID-19, while also preparing to combat emerging coronaviruses in the future. The supporting team assembled from the four research institutions includes: Dr. Jonathan Bohmann and Dr. Hakima Ibaroudene, SwRI; Dr. Luis Martinez- Sobrido, Texas Biomed; and Dr. Stanton McHardy and Dr. Doug Frantz, UTSA.

#### **ROLE OF FURIN**

Dr. Diako Ebrahimi and his team at Texas Biomed are studying the role of the protein FURIN in COVID-19 and how it is potentially impacting individual responses to the virus. The five-lab research team is working to understand the interaction between the SARS-CoV-2 spike protein and host factor FURIN with the ultimate goal of developing inhibitors to stop this interaction, thus blocking viral infection. SARS-CoV-2 uses FURIN, a human protein, to better infect cells in our body. There are FURIN genetic variations that increase the risk of cardiovascular diseases and also potentially lead to severe COVID-19 symptoms and higher mortality rates. The team is initially studying the role of FURIN genetic variations in greater mortality rates among individuals with underlying cardiovascular conditions, with the ultimate goal of blocking the interaction between SARS-CoV-2 and FURIN. Research results also have application to combating the next novel coronavirus, HIV, and other infectious diseases.



Supporting research teams are led by Dr. Jonathan Bohmann, SwRI; Dr. Zhenming Xu and Dr. Dean L. Jr. Kellogg, UT Health San Antonio, and Dr. Stanton McHardy and Dr. Doug Frantz, UTSA.

> Faculty members at the Graduate School of Biomedical Sciences at UT Health San Antonio are working on cutting-edge research in areas such as cancer, heart disease, and neurodegenerative disorders.



## San Antonio Life Science Landscape

### Partner Perspective Southwest Research Institute

### SwRI Bioreactor Propagates Cells for Personalized, Regenerative Medicine

Imagine turbocharging your body's own defenses, using customized cells to attack a specific disease or repair an injury. That type of regenerative therapy could revolutionize how we treat diseases using a patient's own immune or stem cells to fashion targeted treatments. For instance, a patch of stem cells could be used to repair a heart valve. T-cells in our immune system could be modified to seek out and destroy cancer cells.

The promise of personalized, regenerative medicine is limited, in part, by scale. For example, only about 100,000 cells with regenerative potential can be harvested in an autologous or self-donation, but effective treatments often require a billion cells for a single dose, requiring a 10,000-fold increase for clinical applications. Existing technologies do not meet the practical clinical needs for cell manufacturing. These applications typically require an expensive, labor-intensive cell culture process in high-cost cleanroom conditions. Now, there's a new option.

Biomedical engineers at Southwest Research Institute have created a novel cell expansion bioreactor to propagate cells, which increases yields while reducing costs. Fabricated using 3D printers, these single-use scalable devices can expand cells with minimum human interaction in a low-cost cleanroom. SwRl is working with collaborators to create a standalone, programmable closed-loop cell expansion platform about the size of a minifridge to continuously propagate cells using our novel bioreactors. Much like a single-serve coffee maker can brew a variety of beverages using K-cup® pods, this turnkey perfusion-based "cell maker" system can propagate a variety of different types of cells and cell-derived biologics using SwRl's single-use bioreactors.

SwRI has received funding from the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), the Advanced Regenerative Manufacturing Institute (ARMI), the Medical Technology Enterprise Consortium (MTEC) and the Food and Drug Administration (FDA) to demonstrate the technology by propagating T-cells for immunogenic therapy of cancers and mesenchymal stem cells (MSC) to treat age-related degenerative diseases.



#### **Bioreactor Design**

Through internally funded research, SwRI designed, developed and prototyped the bioreactor for T-cell and stem cell expansion. The patent-pending, disk-shaped design features tightly packed, interconnected spherical voids, providing a large surface-to-volume ratio for growing profuse quantities of cells. Its unique structure facilitates automatic control and delivery of nutrition and oxygen to cells.

The bioreactor can grow "suspension" cells, such as disease-fighting white blood cells known as T-cells that can be engineered into T-cells with chimeric antigen receptors (CAR). These CAR T-cells can identify and kill cancer cells. The device also expands "adherent" cells, which include stem cells and primary cells such as those from bone, skin or muscle. The system can also manufacture cell-derived biologics to support gene therapy, therapeutic exosome, recombinant protein, and cell-based vaccine applications. Using a 3D commercial printer, we created production-ready bioreactors of different sizes with the same internal structure. This maintains the cell expansion process from discovery to development and manufacturing, reducing the costs involved to move into the commercialization phase. The device is made of a biocompatible material used in many FDA-cleared or-approved medical devices.

SwRI has developed a proprietary technology to produce the bioreactor with a smooth surface suitable for cell growth. We are currently establishing cleanroom fabrication and radiation sterilization procedures for the bio-reactor to meet the device quality and safety levels needed for clinical cell manufacturing.

#### Turnkey Technology

SwRI's bioreactor facilitates pump-driven perfusion flowbased cell cultures. Perfusion technology mimics the human circulatory system to provide nutrition and oxygen to cells to support growth. Over long periods, a week or two, these systems culture cells continuously, providing the cells with fresh media and removing waste, similar to the circulation system in our bodies.

We are developing a turnkey, standalone system about the This includes a temperature-controlled incubator and a

pump — like a heart — to deliver media to the cells inside the bioreactor. An oxygenator functions like our lungs, refreshing the oxygen concentration and removing carbon dioxide based on the "breathing rate" of the cells. We conducted computational fluid dynamics simulations to demonstrate the media perfusion flow profile across the bioreactor. We enhanced the system with a programmable controller to automate the nutrition and oxygen delivery for cell propagation. And we are integrating the bioreactor with tubing, a media storage bag and a waste collection bag to form a closed, single-use package that can be installed into the perfusion unit.

Perfusion bioreactors offer several advantages over traditional batch bioreactors in terms of scalability. For one, perfusion bioreactors provide a large surface area for cell growth with a relatively small footprint. For example, our 8-inch diameter bioreactor with a 25,000 cm<sup>2</sup> cell surface area has the same cell production capacity as square table. These bioreactors also need less expensive cell culture media and labor to operate, significantly operating costs while producing the same yield.

#### **Tomorrow's Medicine**

When complete, SwRI's automated bioreactor-based system will offer a variety of cell culture surfaces based on specific needs. For example, three bioreactors with cell culture surface areas of 250, 2,500 and 25,000 cm<sup>2</sup> can replace 125 manual-operation flasks, to propagate 1 billion cells. At the end of this program, a sterile fabricated bioreactor, integrated with a programmable perfusion system, will be available for clinical cell manufacturing. This technology will support cell and gene therapy, while promoting San Antonio as a hub for regenerative and precision medicine.

SwRI's disk-shaped bioreactor features tightly packed, interconnected spherical voids, providing a large surface-to-volume ratio for growing abundant quantities of cells.

Advanced regenerative medicine therapies are exciting research topics, with more than 1,000 stem cell therapies currently in clinical trials. Applications include treating cancers, diabetes, traumatic brain injuries, and Alzheimer's and Parkinson's diseases. The cells can also be used to treat spinal cord injuries, heart disease and wounds. Additional applications range from baldness to strokes, muscular dystrophy learning disabilities and more.

Already, the newly-established xCellerate Biotech Inc. (XBI) licensed the bioreactor technology for T-cell manufacturing. Future plans include establishing a manufacturing facility in San Antonio to produce the cell expansion bioreactor and generate supplies for the biopharma industry worldwide. Meanwhile, SwRI continues to seek companies interested in commercializing the bioreactor technology for other applications. SwRI is developing devices and technology that will make growing cells and biologics more efficient and effective, enabling the practical use of tomorrow's personalized, regenerative medicine.





## Fighting A Global Threat with Texas-sized Solutions

In 1976, Steve Jobs and Steve Wozniak founded Apple Computers; the United States celebrated its bicentennial; the Viking 2 landed on MARS; Jimmy Carter was elected president, and a major new disease was uncovered – and it wasn't HIV/AIDS. Acquired Immunodeficiency Syndrome caused by the Human Immunodeficiency Virus would not be named for another five years.

Ebola virus disease, known then as Ebola hemorrhagic fever, was discovered in 1976 and named after the Ebola River near Yambuku in the Democratic Republic of Congo – one of two locations where the first outbreaks occurred. Ebola virus belongs to a family of hemorrhagic fever viruses known to cause damage to multiple organs resulting in death in many instances.

According to the World Health Organization, Ebola Virus disease has a fatality rate around 50%, with some outbreaks seeing a 90% fatality rate. Ebola virus has killed nearly 13,000 people; however, the 2014-2016 outbreak in west Africa killed more than 11,000 of those people, making it the single most deadly Ebola virus outbreak in its 44-year history.

More than 8,000 miles away from its origin, in 1976, Texas Biomedical Research Institute was nearly 25 years away from opening the only privately-owned biosafety level 4 laboratory in the country and becoming one of only seven national primate research centers in the country – the only place in the world with these two resources on one campus and both critical infrastructure assets that would be needed in the fight against infectious diseases, like Ebola. No one would have guessed that the Institute's 1200-square-foot BSL-4 lab built in 1999, along with the establishment of the Southwest National Primate Research Center established in 1999, and a small ensemble of scientists would become the epicenter of Ebola's downfall.

In 2014, when Ebola became a household name due to both the sheer number of deaths and the fact that Ebola had jumped continents, impacting people in Europe and the U.S., Texas Biomed had been studying the virus and its sister hemorrhagic fever viruses for nearly a decade.

The Centers for Disease Control and Prevention (CDC) classified Ebola as a Category A Bioterrorism Disease. That means the virus can be easily transmitted from person to person, results in a high mortality rate, could cause public panic and social disruption, and requires preparation for a response. Texas Biomed's BSL-4 lab was built for the express purpose of studying bioterror agents, such as Herpes B Virus, which lent itself well to studying hemorrhagic fever issues. "Texas Biomed's mission is to discover and share critical breakthroughs needed by scientists to help protect you, your families and the global community from the threats of infectious diseases", explained Dr. Larry S. Schlesinger, President/CEO of Texas Biomed. "The Institute's efforts with Ebola virus disease is an excellent example of the power of collaborative science and the value of investing in necessary resources to conduct innovative research from basic discovery through to clinical studies and ultimately patient care."

Around 2004, scientists at Texas Biomed had put their small lab to work studying hemorrhagic fever viruses, how they infected cells, replicated, mutated and most importantly, how they impacted living organisms – all in an effort to find weaknes and exploit them. Over the next 10 years, the lab would not only enable basic scientific research but would stand up a contract research arm that would facilitate collaborative scientific study on a number of vaccines and, more recently, therapeutics.

By 2014, collaborating with scientists worldwide, Texas Biomed would screen hundreds of drugs as potential antiviral therapies and vaccines and were continuing their efforts to test drug and vaccine candidates, some of which would be deployed in that 2014-2016 outbreak and subsequent outbreaks. These therapies were tested in animal models developed at Texas Biomed for the specific purpose of finding a cure and a vaccine for hemorrhagic fever viruses.

In mid-August 2019, human clinical trials were halted in yet another Ebola epidemic in the Democratic Republic of Congo that to date has claimed more than 2,100 lives. The findings



resulted in the discontinuation of two of the drugs in the trial. Future patients were randomly assigned to receive either REGN-EB3 (Regeneron) or mAb114 (Ridgeback Biotherapeutics) in an extension phase of the study, as these showed to be most promising. Texas Biomed scientists in the Institute's Biosafety Level 4 contract research program conducted preclinical testing of several of the compounds in the trial, working with Regeneron and the Biomedical Advanced Research and Development Authority (BARDA).

"Preclinical data derived in part at Texas Biomed on three of the four drugs showed each of these compounds to be efficacious to some degree," explained Ricardo Carrion, Jr., Ph.D., Professor and Director of Texas Biomed's BSL-4 Contract Research Program. "These studies are excellent examples of how imperative preclinical animal model studies are in order to move drugs forward. And, it is important we continue studying the underlying mechanisms behind the virus to develop even better therapeutics. Having more than one therapy against a disease is always the best option, so further studies should continue."

Over the years, the Institute has partnered with pharmaceutical companies, the Department of Defense and the National Institutes of Health on dozens of Ebola virus research studies and continues these studies today. Texas Biomed is a leader in a global scientific movement that aims to move discovery into patient care faster by fostering both cutting edge, basic science and preclinical, regulated studies as our unique, nimble business model. It is this type of collaborative scientific environment that has produced relatively short-term results in finding drugs and vaccines for Ebola virus. In fact, the U.S. Food and Drug Administration approved its first Ebola virus vaccine cause by Zaire ebolavirus in December 2019, and clinical trials on antiviral drugs are ongoing. Preclinical work, like that done at Texas Biomed on some of the predecessors to this vaccine, helps pave the way for these vaccine developments to occur. It is this type of cooperative effort that will move all science and thus human health forward faster, as the current COVID-19 pandemic has shown the need for.

"It is exciting that we are moving closer to a potential cure for Ebola virus, and we are simply proud to have played a role in working with the organizations developing these therapies" said Dr. Carrion. "We are motivated by the promise of these drugs and are happy to see that patients are recovering, as that is always the goal of our science – to positively impact human lives."



### Data, lots of it, may detect who will have dementia and what type

What if, by inputting information about dementia and a patient into a supercomputer and crunching the data, a treatment team could quantify the individual's risk of developing the disease?

And what if, based on the results, the team could diagnose which type and subtype of dementia that the patient might develop?

And what if the team could prescribe lifestyle changes and drug therapy specifically geared for that subtype to prevent it?

That's the ambitious vision of the future held by Mohamad Habes, Ph.D., director of the Glenn Biggs Institute neuroimaging core at UT Health San Antonio.

Dr. Habes coauthored a paper published this year in the journal Biological Psychiatry that reviewed 29 studies of subtypes of multiple neurodegenerative diseases. These included Alzheimer's disease, Parkinson's disease, frontotemporal dementia and Lewy body dementia. The team also reviewed studies of general brain aging not associated with a disease diagnosis.

#### Clustering information to increase diagnostic power

"In this paper, what we show is that there are atypical presentations of early Alzheimer's and other diseases," Dr. Habes said. "If a patient is at risk to develop a disease, and we use MRI (magnetic resonance imaging) and PET (positron emission tomography) to image that patient, we can then utilize high-dimensional clustering to group the patient into a specific subtype."

The MRI and PET technologies have existed for decades, but the data that can now be gleaned from each image is greater and computing power is commensurately higher. This is an age of machine learning and artificial intelligence. High-dimensional clustering is the concept of bringing multiple dimensions of information together to compute a patient's disease state. "Just think of two dimensions of a picture, extending to three

#### **Guiding treatment**

The bottom line is precision medicine, Dr. Habes said. "Not all people are aging in the same way, and there are a lot of factors that lead to different aging trajectories among individuals," he said. "We will use neuroimaging together with machine learning as a tool to predict and hopefully guide treatment for Alzheimer's disease and these other disorders."

The Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases was established at UT Health San Antonio in 2017. The founding director is Sudha Seshadri, M.D., a leading Alzheimer's disease clinician-researcher and senior investigator with the Framingham Heart Study. The Biggs Institute is dedicated to providing comprehensive care while advancing treatment through education and discovery.

The institute is named for Glenn Biggs, a prominent figure whose leadership influenced economic development across San Antonio. When he was diagnosed with Alzheimer's disease, he and his family struggled to find comprehensive care. This search led him to approach UT Health San Antonio President William L. Henrich, M.D., MACP, and many other community leaders to address the need for a comprehensive center dedicated to understanding Alzheimer's disease.

Dr. Habes joined the Biggs Institute in 2019 from the University of Pennsylvania. His research is supported by National Institutes of Health grants. While the Biggs Institute neuroimaging core currently leverages the Texas Advanced Computing Center at The University of Texas at Austin, Biggs investigators are in the process of building the institute's own high-performance.

dimensions, and then to more and more," Dr. Habes said. "By doing that, you have a better insight, a better representation of the problem, when you have more information about it."

#### **Broadening the datasets**

It is important to incorporate all findings made in past studies, such as the observation that aggressive hypertension treatment might help prevent cognitive decline. It is just as important to broaden the data to include groups such as Hispanics, who have been significantly under-represented in research of Alzheimer's disease and related disorders to date.

"High-dimensional clustering is a research area that is very hot," Dr. Habes said. "Our paper summarizes the work that has been done so far, and we offer advice on how to go forward, combining different levels of data for research projects in the future."



## The Center for Innovative Drug Discovery: A Collaboration Unlike Any Other

Drs. Doug E. Frantz and Stanton F. McHardy have both lost family members to cancer. Armed with personal motivation, scientific expertise and a collaborative mindset, the two UTSA professors are working to discover cancer treatments at the Center for Innovative Drug Discovery (CIDD), a joint venture between UTSA and UT Health.

Their collaboration is unlike any other in the country and is composed of two facilities: A Medicinal Chemistry and Synthesis Core Facility housed at UTSA and a High-Throughput Screening (HTS) Facility located at UT Health that is under the direction of Dr. Matt Hart. These two resources allow scientists from different disciplines, such as chemistry and biology, to work together, creating a synergistic strategy to address a drug discovery unmet medical need. These multi-disciplinary collaborations create a strong research platform that has ultimately increased the competitiveness of state and federal extramural grant applications.

Dr. McHardy and Dr. Frantz have distinct professional and academic backgrounds that complement each other and result in the CIDD's capabilities, not normally found in a single academic environment. Dr. McHardy is an associate professor of chemistry and the CIDD director. Dr. Frantz is the Max and Minnie Tomerlin Voelcker Distinguished Professor of Chemistry, co-founder of the CIDD, and was recently awarded a substantial grant to establish the Max and Minnie Tomerlin Voelcker CIDD Preclinical Pharmacology Core for Accelerated Drug Discovery, which will allow local researchers to rapidly identify the best drug leads to move forward to the clinical phase here in San Antonio. Both Dr. McHardy and Dr. Frantz also have extensive experience working in the pharmaceutical industry, Pfizer and Merck respectively, that gives them a unique perspective and advantage over other academic drug discovery endeavors.

Through this unique collaboration, the CIDD provides a diverse array of core facilities and expertise to facilitate the translation of basic scientific discoveries into tangible pre-clinical candidate drugs that can be further developed into clinical therapies for human disease. The Center's mission is to catalyze collaborations with investigators by providing high-quality, industry-level services and expertise related to small molecule drug discovery and pre-clinical development.

The collaborative medicinal chemistry strategy is focused on the translation of small molecules into tangible drug candidates that can be advanced toward clinical studies. Medicinal chemistry is a core discipline in the drug discovery process and is applicable across all therapeutic areas. This allows the CIDD to create numerous productive research collaborations in areas such as cancer, infectious disease and diabetes, as well as psychotherapeutics and neurodegenerative central nervous system (CNS) disorders.

This strategy has allowed the CIDD to collaborate with the top researchers in the state and nation to build multi-disciplinary expertise and strengthen programs, which in turn has added value to the UTSA mission through successful grant funding and valuable research experience for UTSA students at both the undergraduate and graduate level.

#### Services provided by the CIDD include:

- consultation and hands-on assistance in the design, development and implementation of assays suitable for HTS, including assay validation, optimization and miniaturization
- expression and purification of proteins for small molecule discovery and structural biology studies, which include in silico docking programs to optimize drug candidates
- screening of compound libraries using cell-based highcontent imaging, cell-based conventional, or purified component-based screens
- medicinal chemistry optimization of lead compound drug candidates through structure-activity relationship studies
  custom synthesis and consultation. CIDD also provides
- consultation and support on program strategy design from



core directors who have over 40+ years of combined experience in moving small molecule compounds through all stages of the pre-clinical drug discovery process both in pharmaceutical industry and academic environments.

These services also integrate closely with Structural Biology and Biophysical Core Facilities at UT Health to further enhance and optimize potential therapeutics.

Dr. Frantz and Dr. McHardy's teams work on collaborative programs in cancer, neuroscience, infectious diseases and diabetes among other areas. In addition to empowering the translational components of academic research programs in South Texas and interfacing with the growing biotechnology/ pharmaceutical industry in South Texas, CIDD is also leading the effort to establish new Certificate and MS training programs to build a local workforce in all areas of drug discovery. Since its establishment in 2012, the CIDD core facilities have successfully participated in over 50 novel drug-discovery programs across a range of therapeutic areas, which has resulted in over 25 peer-reviewed publications, over 15 invention disclosures and more than \$17 million in extramural funding.

Dr. Frantz and Dr. McHardy admittedly touch any therapeutic area that they can get our hands on and know that they have developed a unique gem in the state of Texas. The CIDD's efforts are further enhanced by the partnerships across the four institutions that are part of the San Antonio Precision Therapeutics (SAPPT), making the CIDD a collaboration like no other.

> Since 2012 the CIDD has successfully participated in more than 50 novel drug discovery programs across a range of therapeutic areas.

## COVID-19 Response



### Southwest Research Institute

• Using Department of Defense supercomputers and Southwest Research Institute's 3D drug screening software tool, Rhodium<sup>™</sup>, SwRI is virtually screening millions of drug compounds to search for and test possible treatment options for COVID-19. The supercomputers speed up the screening process, allowing for the evaluation of 40 million therapeutic compounds per week.

• The ISO 17025 A2LA accredited Particle Science and Technology Laboratory at Southwest Research Institute has expanded its services to include respirator and mask testing in response to the COVID-19 pandemic. The testing allows health care and other organizations to evaluate respirators, surgical face masks and filtration materials to ensure they meet particle filtration standards. Recent testing at SwRI revealed eight out of the 11 KN95 respirator samples submitted by clients were counterfeit.

### **Texas Biomed Research Institute**

• The current COVID-19 pandemic underscores the importance of Texas Biomed's mission to protect the world from the threat of infectious diseases. The pandemic has quickly galvanized the scientific team and engaged the Institute's supporters to mobilize resources and aid the world in finding interventions to fight COVID-19. Texas Biomed has successfully responded to the need for COVID-19 research with more than two dozen COVID-19 projects underway, as well as partnerships with review by the FDA.

• The Institute's initial COVID-19 project was a campus-wide effort to identify an appropriate pre-clinical animal model for scientists completed a study evaluating three nonhuman primate (NHP) species, including both young and old animals development of COVID-19 disease. Over the course of the promise as animal models for COVID-19 disease studies moving in vaccine efficacy and safety preclinical studies.

• To prevent the spread of COVID-19 in the workplace, frequent surface disinfection is necessary in common areas. Southwest Research Institute is part of a project team building a disinfecting autonomous mobile robot. SwRI engineers are developing path planning software for the robotic arm of the Mobile Autonomous Industrial Disinfector (MAID), which will help the robot navigate the space it is cleaning. The system will eliminate the need to expose a person to a potentially contaminated environment.

 Southwest Research Institute's Manufacturing Technologies Department and the Texas Manufacturing Assistance Center (TMAC) South-Central Region are working with the San Antonio Manufacturing Association, helping local companies produce personal protection equipment (PPE), including shields for the University Health System in San Antonio. SwRI is also helping a local manufacturer augment throughput for production of disinfecting robots and supporting production of consumables and spare parts for ventilators.

• Texas Biomed scientists added another tool to the COVID-19 toolbelt, validating a small animal model for studying SARS-CoV-2. Researchers at the Institute were among a limited group of scientists nationwide given early access to newly developed transgenic mice that express the human angiotensin can be used as a small animal model to assess SARS-CoV-2 infection. Texas Biomed scientists not only found that the infection but also discovered key indicators of an inflammatory immune response (activation of the immune system) and were among the first to discover that this transgenic mouse succumb

• Through the process of reverse genetics via bacterial artificial chromosome (BAC), scientists at Texas Biomed have also created a recombinant SARS-CoV-2, which is a cloned virus hamsters. This is the first SARS-CoV-2 study using this approach, vaccines to combat the disease.

UT Health San Antonio led one of the nation's leading COVID-19 vaccine trials with Remdesivir and was the first in San Antonio to administer the vaccine.

### **UT Health San Antonio**

• UT Health San Antonio is on the front lines of the COVID-19 response, fighting the disease from all sides. The university's researchers are consumed by work on a vaccine and antivirals, its health care workers continue to spend untold hours treating the sickest of our region's patients and testing to avoid further spread, and its educators have not paused in the least as they provide a first-rate curriculum for tomorrow's leaders in medicine, dentistry, nursing, other health professions and scientific research.

• UT Health San Antonio scientists are using super-resolution microscopes to visualize how SARS-CoV-2 enters the heart's muscle cells, which are called cardiomyocytes. The virus attacks structures called mitochondria – cellular power plants that produce energy, enabling the cardiomyocytes to beat and pump blood. The lead researcher for this project is also the principal investigator of a \$200,000 grant awarded by SAPPT to study the cause, prevention and treatment of multi-organ failure during sepsis.

## The University of Texas San Antonio

• UTSA's Doug Frantz, Chemistry and co-founder of the university's Center for Innovative Drug Discovery, is screening small molecule libraries to identify compounds that could potentially be developed into a coronavirus treatment. cells infected with SARS-CoV-2 will be pretreated with the compounds designed at UTSA. Researchers at UTMB Galveston aim to provide preliminary data from these tests shortly.

• UTSA researchers have developed a new breathing tube designed to solve the problem of instability and tissue damage from the long-term ventilation of COVID-19 patients and emergency medicine. Creators of this new breathing tube include David Restrepo, Mechanical Engineering, R. Lyle Hood, David Berard.

• UT Health San Antonio is supporting multiple vaccine development studies. A team from the Joe R. and Teresa Lozano Long School of Medicine seeks to isolate antibodies that neutralize SARS-CoV-2. People who had the infection and recovered from it make specific antibodies. The team is obtaining samples from these individuals and studying the antibodies. The researchers are studying the antibodies' chemical footprints to learn which antibodies inhibit the virus and which do not. The team is working with colleagues at Texas Biomed, where biosafety level 3 and 4 labs enable scientists to work with live virus.

• UT Health San Antonio has been integrally involved in testing the anti-viral drug Remdesivir for hospitalized COVID-19 patients, enrolling the largest number of patients worldwide in the second phase of the trial. Thomas Patterson, M.D., Chief of the Division of Infectious Diseases in the Long School of Medicine, is leading a local study site of the Adaptive COVID-19 Treatment Trial (ACTT) with clinical partner University Health System.

• A team of UTSA researchers has teamed up with San Antonio College in a study investigating the attitudes and behaviors of college students amid the coronavirus pandemic. Thankam S. Sunil, Xiaohe Xu and Eric C. Shattuck from the Institute for knowledge, attitudes and behaviors related to COVID-19.

• The COVID-19 Resources & Recovery Site takes the power of crowdsourcing and created a tool to help the public during Dr. Amina Qutub, Biomedical Engineering, and Dr. Hongjie Xie, Geological Sciences, led efforts to rapidly develop the site.

## San Antonio Bioscience Ecosystem

Ongoing research in Texas Biomed's BSL-4 lab is focused on high consequence pathogens and bio threats, like Ebola, and the organization's AIDS Research Program.

> TO LEARN MORE ABOUT THE SAN ANTONIO REGION, VISIT SANANTONIOEDF.COM

At the intersection of innovation, manufacturing and science, the comprehensive bioscience ecosystem in San Antonio is uniquely positioned to grow. It contains end-to-end expertise to carry an idea from conception and discovery through formulation and testing to clinical trials and bedside delivery. Combining this expertise with our enthusiastic approach to collaboration allows our bioscience community to explore all possibilities and opportunities in precision therapeutic medicine.

Further, San Antonio's demographic and ethnically diverse population makes our city a prime location for developing effective and efficient precision

### The bioscience industry in San Antonio includes all organizations that are focused on the research and/or commercialization of innovations that are designed to improve quality of life.

therapeutics models that can be applied globally. San Antonio currently reflects the future demographic makeup of the nation. Of the city's more than 2.5 million residents, 65% are Hispanic, a ratio that has long been predicted to be the national norm by 2050. What can be modeled, tested and proven in San Antonio can be expected to be successful across the U.S.

San Antonio is also the home of Military Medicine. A critical component to San Antonio's advantage, the advanced research and technology taking shape at our military installations benefits our own research community, innovates processes and procedures, and provides technological advances across industry. More than 50% of military personnel stationed in San Antonio decide to stay when they retire or separate from active duty, contributing to a brain gain with their extensive training, education and medical experience. The collaborative nature of industry leaders fuels our breakthroughs and personalized, or precision therapies in: Human performance, infectious diseases, cancer, aging, obesity, and diabetes. The impact of these advances reaches far beyond our city limits.

In addition to the partner organizations that comprise SAPPT, San Antonio's bioscience ecosystem includes military, education, and private sector assets.

SAPPT is not the first collaboration between SwRI, Texas Biomed, UT Health SA, and UTSA. Founded in 2019 The Vaccine Development Center of San Antonio

promotes collaboration among these four research institutions in infectious disease research and vaccine development in order to facilitate new discoveries and eliminate duplication of resources.

Dr. Joanne Turner, Executive Director of Vaccine Development Center of San Antonio, expressed enthusiasm over the additional partnership opportunities that SAPPT provides. "The Vaccine Development Center of San Antonio's mission is to support communication on vaccine research, perform public outreach and education on vaccines with city partners, and to fund innovative collaborative research on vaccine development in San Antonio. We are excited to partner with SAPPT to fast track research efforts."



#### **By The Numbers**





**IOF6 SAN ANTONIANS** WORK IN BIOSCIENCE & **HEALTH CARE** 



## **Home of Military Medicine**

#### **INNOVATIONS**

The innovation taking place at our military installations and at Brooke Army Medical Center, the largest military health care organization within the Department of Defense (DoD), benefit the research community and provide technological advances for the entire industry.

#### WORKFORCE

More than 50% of military personnel stationed in San Antonio decide to stay when they retire or separate from active duty. These transitioning service members have extensive training and education, the largest group citing medical experience.

#### FUNDING

Our military presence also gives the local industry greater access to federal funding and to the DoD contracts.

#### TALENT PIPELINE

Twelve local universities and colleges offering 92 post-graduate bioscience programs serve as key sources for San Antonio's R&D and private sector bioscience employers filling high demand occupations. Work-based learning opportunities like job shadows, internships, and summer camps beginning in middle school provide early exposure to career pathways that exist in San Antonio's bioscience sector.

#### **PRIVATE SECTOR**

San Antonio is home to the largest bioscience headquarters in Texas: 3MKCI. The city also boasts a number of other large companies and services centers responsible for thousands of jobs and hundreds of millions of dollars in value creation.

# \$1 Billion IN FEDERAL R&D EXPENDITURES

50,000+

#### **NEW JOBS IN THE BIOSCIENCE INDUSTRY IN THE LAST DECADE**

MORETHAN 3.300

SAN ANTONIO BIOSCIENCE ECOSYSTEM HOME OF MILITARY MEDICINE



(AS OF 2018)





MDs AND PhDs

## San Antonio Bioscience Forecast



In the next 5 years, San Antonio's bioscience sector is projected to grow 16.2%, outpacing the national growth rate of 11%.

Photo courtesy of Southwest Research Institute

In the San Antonio region, bioscience as a regional opportunity is not new. What is new and unique are the shared goals and collaboration among the area 's leading bioscience organizations, working together to demonstrate the industry's leading position in precision therapeutics.

The world is recognizing transdisciplinary collaborations, and efforts such as those that SAPPT are spearheading are needed to address the grand challenges needed now more than ever. Effective community and public health initiatives require a deep understanding of the human genome and how a body responds to varying treatments. The efficacy we need – and the future of medicine – can be found in precision therapeutics.

As personalized medicine becomes a more mainstream approach to health and wellbeing, the industry needs to be able to develop it with 100% certitude. That confidence in the results requires the talent and abilities inherant in the collective power of research. In addition, San Antonio is a living lab of what U.S. demographics will begin to look like. Harnessing all of the region's expertise provides the opportunity to get ahead of the curve and understand medical problems before the demographic surge.

Ultimately, the synergy among SAPPT organizations and what we can do together will be the gamechanger.



"Excitment springs from the leaps we can make in science by integrating normally distinct disciplines."

> LARRY SCHLESINGER, M.D. PRESIDENT & CEO, TEXAS BIOMEDICAL RESEARCH INSTITUTE



"In San Antonio, there's an eagerness to collaborate. Our leaders proactively build bridges and look for opportunities to work together. That's the harbinger of what's to come – the future approach to medicine."

> WILLIAM L. HENRICH , M.D., MACP PRESIDENT, UT HEALTH SAN ANTONIO

"SAPPT can, should and needs to focus on precision therapy and disrupt current processes. Only then can we leverage collective and complementary expertise for improved health."



#### TAYLOR EIGHMY, Ph.D.

PRESIDENT, THE UNIVERSITY OF TEXAS AT SAN ANTONIO

"Our region offers every kind of expertise needed: discovery processes, formulation of drug therapies, lab testing, clinical trials and bedside delivery. We have the greatest possibility for success when all this expertise works seamlessly as it is does among the SAPPT organizations."



#### ADAM L. HAMILTON, P.E.

PRESIDENT & CEO, SOUTHWEST RESEARCH INSTITUTE



# Acknowledgements

SANANTONIOEDF.COM SAPPT.ORG

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