Good day, LA BioMed!! And welcome to the first issue of BioBeat, the Science Newsletter for LA BioMed.

With this newsletter, we will promote the exciting research being done at our institute by our colleagues. We will showcase the many faces of our institute, in the section Faces of Excellence, in which the people doing the science will be portrayed, be they trainees, technicians or support personnel. In addition, look out for the publications coming out of our laboratories, grouped by the 8 strategic themes of the institute. Last, but not least, the newsletter will be open to any research-related announcements such as unique funding opportunities, important conferences or seminars, or ground-breaking developments on campus and around the world.

For this inaugural issue of BioBeat, what better way to start than by portraying the three investigators honored at the 2017 LA BioMed Gala, Doctors Casaburi, Chang and Yeaman. They are prime examples of the culture of excellence and innovation of our institute, covering fundamental aspects of science and their translation and commercialization for the good of mankind. Also, as our first Faces of Excellence, be introduced to Dr. Liana Chang, a post-doc in Dr. Yeaman’s lab.

Without further ado, welcome to BioBeat!!

Yours in service,
Quim Madrenas, CSO

From the CSO’s Desk

Improving the Lives of People Living with COPD

“This is our next mission – to show that exercise rehabilitation will make COPD patients live longer.”

For Richard Casaburi, PhD, MD, his groundbreaking research began with a simple but profound finding from exercise studies. Working with others, he documented the fact that breathing during exercise becomes easier as people exercised more.

“We came to recognize that exercise training modified the way the body responds to exercise in very profound ways,” Dr. Casaburi said. “One particular finding was that, after people engaged in an exercise program, they needed to breathe less.”

He had conducted his study with healthy people, and he wondered whether the same might be true among people who had breathing problems, especially among those living with Chronic Obstructive Pulmonary Disease (COPD), now the third leading cause of death in the U.S.

Many others were skeptical that exercise alone would be enough to improve COPD patients’ breathing. But Dr. Casaburi and his colleagues moved ahead, putting people living with COPD through prescribed exercise regimens on stationary bicycles and treadmills.

Over time, he found their breathing greatly improved. People who had once struggled to climb stairs or walk long distances could manage these more easily, and with less shortness of breath. In 1995, Dr. Casaburi published what he considers among his “most impactful” research paper, a study in the American Journal of Respiratory and Critical Care Medicine, reporting that exercise could improve breathing in patients with severe COPD.

“He made history and his efforts helped to make pulmonary rehabilitation the standard of care around the world,” said Mary Burns, RN, MS. She was one of the early adopters of pulmonary rehabilitation and worked with Dr. Casaburi on this seminal study. She has become one of his biggest supporters.

Despite these conclusive findings, Dr. Casaburi said only about 3% of the patients who are eligible have access to exercise rehabilitation. Expanding access will require proving that exercise rehabilitation not only improves the quality of life but actually extends life.

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Dr. Casaburi and his colleagues at National Jewish Health in Denver and the University of Illinois at Chicago are seeking a $40 million NIH grant for a multicenter study involving 2000 COPD patients seeking to determine whether providing exercise rehabilitation as they leave the hospital after a COPD flare-up will prolong their life and prevent their return to the hospital.

“This is our next mission – to show that exercise rehabilitation will make COPD patients live longer,” he said.

Seeking the Genetic Causes of COPD

Dr. Casaburi and his colleagues in the Rehabilitation Clinical Trials Center have completed more than 75 clinical research studies, including participating in three major NIH multicenter projects. One of those is the COPDGene® Study, the largest study ever to investigate the underlying genetic factors of COPD. Through the enrollment of over 10,000 individuals, the COPDGene® Study aims to find inherited or genetic factors that make some people more likely than others to develop COPD. With the use of CT scans, COPDGene® also seeks to better classify COPD and understand how the disease may differ from person to person.

At LA BioMed, Dr. Casaburi and his colleagues have enrolled more than 760 patients in the study, and they have partnered with Matthew Budoff, MD, to provide the CT scans. The study was extended for five years (and may be extended further), so Dr. Casaburi and his colleagues have brought back over 400 of the research volunteers to get more information about how the disease progresses.

Looking to the Future

Dr. Casaburi, along with Dr. Janos Porszasz, established the Rehabilitation Clinical Trials Center at LA BioMed in 1999. He's been working to ensure its future after he retires through the recruitment of pulmonary and exercise specialists, including Harry Rossiter, PhD, and a William Stringer, MD. He has benefitted from private support from Alvin Grancell and Mary Burns, who endowed the Alvin Grancell/Mary Burns Endowed Chair in the Rehabilitative Sciences at LA BioMed, which he holds. He also serves as President of the Pulmonary Education and Research Foundation, a non-profit corporation dedicated to advancing the scientific basis and practice of pulmonary rehabilitation.

Ruey-Kang Chang, MD, is haunted by the memory of an 11-month-old baby boy experiencing repeated seizures when he arrived at Harbor-UCLA Medical Center. The pediatric cardiologist helped diagnose the cause — a genetic heart condition, known as Long QT Syndrome (LQTS). The child survived but he suffered severe brain damage.

“He would have been fine if he had been diagnosed sooner and received the proper treatment,” Dr. Chang said.

He has since developed a device, the QTcheck, to detect LQTS in newborns, and he founded a company, QT Medical, in 2013 to bring QTcheck and other devices to market. QTcheck is about the size of a matchbox and addresses many of the challenges to detecting LQTS, a major cause of Sudden Infant Death Syndrome that is responsible for 300 to 400 deaths in the U.S. each year.

Detecting these electrical abnormalities in a baby's heart is difficult because there are no electrocardiogram (ECG) systems designed for newborns. In addition, LQTS can't be accurately diagnosed until the baby is 2-4 weeks old — usually well after the infant has left the hospital. Once diagnosed, most babies can be treated successfully with a beta-blocker. A small number may need a defibrillator.

“QTcheck is designed with electrodes to fit on a newborn's chest so that it can be used by parents at home,” Dr. Chang said. “Our research has shown that parents who had no prior training or experience could follow the simple instructions for performing the test.”

He's submitted QTcheck to the FDA for approval and is seeking additional NIH funds for a Phase IIb trial to test the market for the device.

“We are hoping to have it on the market in 2018,” he said.

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**Chang, continued**

**Using Technology to Improve Asthma Therapy**

Dr. Chang is also working on four other technologies that are in earlier phases of development, including the Asthmagram, which stems from his and his mother's experiences with asthma.

“Asthma is not a disease you can cure, thus medical therapy is mostly aimed at preventing and relieving symptoms. However, pediatric asthma symptoms are under-reported by the patients and their parents, leading to under-treatment, while adult asthma symptoms are generally over-reported, leading to over-medication,” Dr. Chang said.

To ensure proper treatment, he is developing the Asthmagram to objectively measure the severity of asthma symptoms. This wearable device is the size and shape of a large Band-aid®. It is worn on the neck, above the trachea, for two weeks to record wheezing, coughing and other asthma symptoms.

Armed with this information, Dr. Chang said physicians can more accurately match treatments to the actual symptoms. He formed another company, NeoVative, Inc. to develop the Asthmagram.

**Using Technology to Improve the Quality of Resuscitation in Code Blue Emergencies**

NeoVative is also developing Bluebox to help improve hospitals’ Code Blue emergency responses.

“In a Code Blue emergency resuscitation, there’s often many things happening at the same time, and one person designated to record all of that — on a ‘code sheet’” Dr. Chang said. “The notes that person takes are not very detailed, out of sequence and full of errors.”

Like the black box used in aircrafts’ crash analyses, Bluebox is designed to objectively record all the activities surrounding a patient’s emergency resuscitation in the hospital so that the medical staff can better evaluate their responses in the post-resuscitation debriefing. It is a small device attached to patient's left chest in a Code Blue to record sounds in the room and from the patient, the patient’s chest movement and breathing, as well as the patient’s vital signs, including the ECG.

In addition to these devices, Dr. Chang also holds patents on a device to help prevent SIDS and a more portable and less expensive pulse oximeter to more easily measure oxygen levels in newborns and improve the detection of congenital heart abnormalities.

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**Innovative Solutions for Antibiotic Resistant Infections**

**Michael R. Yeaman, PhD,** pioneers new solutions to meet the growing threat of antibiotic resistant infections. His innovative work has led to completely new types of anti-infective agents and vaccines to meet this challenge to personal and public health. Here are a few of his research projects.

**Turning Test-Tube Science into Live-Saving Treatments**

Dr. Yeaman is Professor of Medicine at the David Geffen School of Medicine at UCLA, and Chief of the Division of Molecular Medicine at Harbor-UCLA Medical Center. His 27 years of research at LA BioMed have led to discovering and translating innovative approaches to address drug-resistant infections. He holds 18 patents, and is founder of two biotech startups: NovaDigm Therapeutics, Inc., which has completed a Phase II clinical trial of its lead vaccine candidate — and Tegos Therapeutics, which develops next-generation agents to defeat deadly infections. Colleagues at LA BioMed who are Novadigm founders also include John E. (Jack) Edwards, Jr., MD, Scott G. Filler, MD and Ashraf S. Ibrahim, PhD.

**Facing the Realities of Resistant Infections**

The research Dr. Yeaman is leading is urgently needed. The U.S. Centers for Disease Control and Prevention (CDC) estimate that more than 2 million Americans suffer from antibiotic-resistant infections each year — resulting in nearly 30,000 deaths. Many more patients suffer prolonged hospital stays and exposure to poorly effective or toxic antibiotics. Estimated costs of drug-resistant infections to the healthcare system range as high as $20 billion per year in the U.S. alone — with up to $35 billion in additional costs to society for lost productivity, according to the CDC. The global impact of drug-resistant infections is many-fold greater still.

**Rethinking Anti-Infective Discovery**

A common misperception is that antibiotics cause drug resistance. The reality is that antibiotics select for microbes that long ago learned how to resist. “We are rethinking antibiotics — to focus on new agents and strategies that enhance the immune system”, said Dr. Yeaman. One example of his field-changing ideas earned him an NIH Innovation Award to find new ways to tame pathogens that otherwise avoid the immune system and cause disease. In this revolutionary work, he found compounds that enhance immunity, restore antibiotic effectiveness and minimize resistance.

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Yeaman, continued

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Making Precision Medicine Personal
Dr. Yeaman is the Principal Investigator of a one-of-a-kind Systems Immunology grant from the NIH that aims to achieve this very goal. His five-year, $10 million multicenter study partners Duke University and Westwood UCLA to unite precision medicine — which aims to target disease-causing microorganisms — with personalized medicine — which customizes treatments to a specific patient. “The history of antibiotic use has been one-size-fits-all. Today, we study features of the immune system in a patient suffering from infection — and those of the microbe causing infection in that patient. From these data, we are creating predictive tools to apply the best antibiotic to treat that specific infection in that specific patient.” His work aims to open the combination lock of patient, microbe and antibiotic that can change a life-threatening infection into a life-saving cure.

Helping the Military Defeat Superbugs
For the Department of Defense, Dr. Yeaman and colleagues are studying whether their new vaccine can protect U.S. Army recruits against MRSA. About 15% of boot camp recruits carry MRSA when they first arrive at camp. After a few weeks of training in close quarters, MRSA can be transmitted to others who have less immunity to MRSA, leading to debilitating infection. In another DoD project, Dr. Yeaman is advancing a new antibiotic he invented to treat one of the most deadly of all infections caused by a pathogen named Acinetobacter.

Uncovering Secrets of Immunity
The research Dr. Yeaman leads is blazing exciting new trails to prevent and treat disease — infection and beyond. “Our work is uncovering previously unknown secrets and dysfunctions in immune response that manifest across many conditions — from infection to autoimmune disease to cancer. By applying this knowledge in new ways, we hope to lead a bold new era of immune health.”

Faces of Excellence

Liana Chan, PhD
Postdoctoral Fellow in Dr. Michael Yeaman's lab

Education
BS in Biotechnology
University of California, Davis, 2005

PhD in Infectious Diseases and Immunity
University of California, Berkeley, 2014

What brought you to LA BioMed?
I met Dr. Michael Yeaman (an LA BioMed infectious disease specialist) at a Gordon conference on Staphylococcal diseases. As a post-doc, I was searching for a lab specializing in my areas of interest. Dr. Yeaman was one of a few researchers studying anti-infectives, immunology and infectious diseases. I asked if he had a post-doc position available or if he could refer me to someone in a similar field.

How do you like working at LA BioMed?
I have been here three years, and it's been a good experience. All the PIs (principal investigators) are collaborative in the infectious diseases department. For instance, Dr. Scott Filler often provides advice on my studies. My current project analyzes the host response to recurrent Staphylococcus aureus skin infection, which is a prevalent disease.

What are your future goals?
I'm hoping to submit additional grants to fund my research. This year, I was fortunate to receive an American Heart Association grant. My goal is to become a professor and conduct independent research projects.


