SPECIAL COVID-19 ISSUE
Several LIMR investigators have rapidly pivoted their research to battle the coronavirus | Pages 2, 3 & 5

ALSO:
Advancing Patient Care Through Research and Physician Training
Page 7

Developing Impactful Research Collaborations
Page 8
LIMR’s Pivot Toward COVID-19

First and foremost, I hope this issue of Catalyst finds you and your family in good health during these challenging times.

While the news about the spread of COVID-19 has been grim, I am excited to report how several Lankenau Institute for Medical Research (LIMR) investigators have pivoted their teams’ attention and considerable expertise to battling the SARS-CoV-2 virus and attenuating its reach.

The work of scientists at LIMR that involves collaborations around the world couldn’t be more crucial. While our colleagues in the clinic continue their heroic fight to save patients stricken by the virus — as of early June, 1,650 COVID-19-positive patients had been treated across Main Line Health — the world’s attention has now turned to science. To all, it’s now apparent that the path out of this pandemic runs through the laboratory.

Throughout modern history, biomedical researchers have pondered, experimented, hypothesized, argued, and bent back over their microscopes, all in an unceasing drive to solve medical mysteries. What causes the onset of disease? Why are some patients more severely affected? What can eradicate dangerous microbes or at least stop them from causing harm in humans? While researchers are not super-human, they do share an important characteristic — one that is particularly useful during difficult times such as these. They are curious.

While others may shy away, biomedical researchers’ natural tendency is to lean in, providing for data, wondering why nature behaves as it does. We need this inquisitive mindset now more than ever.

As the pandemic runs through the laboratory, I am extremely proud of the rapid turn made by our teams whose work is most relevant to these times, highlighting the enormous value of research to solving human health challenges — not only for chronic deadly conditions such as cancer and cardiovascular disease, but also for serious emergent illnesses such as coronavirus infection.

While the work of scientists at LIMR that involves collaborations around the world couldn’t be more crucial, the team at LIMR is also handling the disruptions that the outbreak has wrought on their lives. I am extremely proud of the rapid turn made by our teams whose work is most relevant to these times, highlighting the enormous value of research to solving human health challenges — not only for chronic deadly conditions such as cancer and cardiovascular disease, but also for serious emergent illnesses such as coronavirus infection.

In this issue of Catalyst, you’ll read how several LIMR investigators have turned rapidly to try to solve some of the challenges posed by the coronavirus. You’ll learn about a new antibody testing method, a brand-new way to develop vaccines to fight viruses, promising therapeutic investigations, and basic and clinical research in which faculty are presently engaged — all with the hope of helping to eradicate this terrible pandemic.

You’ll also be among the first to read the results of an important consumer survey about the virus that was conducted by our colleagues at the Main Line Health Center for Population Health Research at LIMR. They surveyed close to 5,600 people around the country, the results of which are giving the research team significant insights into how people are handling the disruptions that the outbreak has wrought on their lives.

I am extremely proud of the rapid turn made by our teams whose work is most relevant to these times, highlighting the enormous value of research to solving human health challenges — not only for chronic deadly conditions such as cancer and cardiovascular disease, but also for serious emergent illnesses such as coronavirus infection. All of us at LIMR thank you for supporting our work, and we hope for your continued health and well-being.

Note: All of the photos for this issue were taken in early March, before social-distancing guidelines were put in place.

Fundraising Challenge Alert

A group of LIMR Board Members — spearheaded by Chairman Peter Havens and his wife Louise, Jonathan Fox and Suzanne Markel-Fox, and Leila Gordon — have generously initiated a 1:1 fundraising challenge match to support LIMR’s COVID-19 Research Fund. Together, they have pledged a gift of $80,000 if an additional $80,000 can be raised by the end of 2020. You can accelerate this important coronavirus research by making a gift to help meet this challenge. For more information on the LIMR COVID-19 Research Fund, see inside back cover.
The researchers at LIMR are using a unique technology pioneered at the Institute that can quickly define and synthesize for study and mass production of SARS-CoV-2 antibodies from patients who have recovered from COVID-19 infection. This powerful technology is part of a clinical trial organized with physician colleagues at Lankenau Medical Center to recruit patients who consent to blood donation for this important work.

Many researchers and commercial interests are touting their antibody tests to COVID-19. But in truth, no one currently knows if the presence of anti-viral antibodies in the blood is a sure sign yet of immunity to coronavirus — and if it could be protective, for how long that immunity may last. Indeed, other kinds of coronaviruses that cause the common cold do not tend to confer long-lasting immunity.

Along with his team members, scientific collaborators and clinical colleagues at Lankenau, LIMR Professor Scott Dessain, MD, PhD, is applying his technology and know-how to clone antibodies from COVID-19 patients whose immune systems successfully defeated the infection. What does an efficient SARS-CoV-2-stopping antibody look like?

The technology being used by Dr. Dessain’s team offers a tool to sift through many antibodies that can recognize the virus and see whether there are any common or special characteristics. “If we found similar antibody patterns in different patients, we may begin to define structural foundations for immunity,” noted Dr. Dessain who holds The Joseph and Ray Gordon Chair in Clinical Oncology and Research. “While such patterns would not be proof of immunity, it could put us on the pathway to discovery, and that’s a step in the right direction.”

Team members have two basic goals. First, they seek to develop a blood test to identify anti-viral antibodies. At present, no test can identify anti-viral antibodies that actually confer protection — these are the most important to define and a key goal of the team’s work. Such a test would be an ideal diagnostic for Main Line Health patients, clinicians and staff members to help allay their fears about the virus.

Next step: Potential therapy?

Beyond simply identifying anti-viral antibodies, the team also seeks to determine if the antibodies they discover could offer an effective route to actually treat COVID-19. As Dr. Dessain notes that while researchers elsewhere are also working in this area, LIMR’s proprietary technology may provide a platform that can more quickly identify and mass produce the best antibodies needed for blood tests and immunotherapies. This technology uses a revolutionary antibody-discovery method invented at LIMR called On-Cell mAb Screening™ (OCMS) that has been applied in other disease settings to rapidly identify and isolate antibodies with the most desirable properties.

OCMS has an impressive track record already, having been used at LIMR to isolate the best patient-derived antibodies ever obtained against polio virus. In fact, these antibodies were designated recently as the International Reference Standard by the World Health Organization (WHO) and other global authorities for batch quality control of Sabin vaccines used to prevent polio worldwide.

Noted Dr. Prendergast, “In applying the powerful thrust of the new OCMS technology developed at LIMR, Dr. Dessain and his team are moving rapidly to illuminate secrets the human immune system has yet to reveal about how to defeat COVID-19. Accessing the antibodies from recovered patients with this technology is a new tool in the armamentarium to eradicate this virus.”

You can help Dr. Dessain and other LIMR researchers as they strive to eradicate the coronavirus.

Please give to the COVID-19 Research Fund. See inside back cover for more.

When the COVID-19 pandemic was prompting governors around the nation to issue urgent stay-at-home orders to their citizenry in March, and U.S. health care providers were rushing to ramp up hospital and treatment protocols, investigators at the Main Line Health Center for Population Health Research (CPHR) at LIMR had an emergency conference call.

During the call, Sharon Larson, PhD, professor and executive director of CPHR, wondered aloud about the overall impact the crisis would have on the lives of those in the community, not just on their physical health, but also on their finances, careers and stress levels.

“We know that many factors contribute to health status,” noted Dr. Larson, who is trained as a psychiatric epidemiologist. “We wanted to get a good idea of how people were handling the situation, because that could better inform Main Line Health clinicians when treating patients both today and tomorrow.”

Founded in 2016, CPHR is a collaboration between Main Line Health and Thomas Jefferson University’s College of Population Health. The research center, which is located at LIMR with the basic and clinical science divisions, seeks to advance the understanding of population health by being a research and educational partner to Main Line Health, informing and assessing initiatives to improve the health status and quality of life in the myriad communities it serves. CPHR investigators spearhead studies that aim to illuminate the underlying socioeconomic challenges inherent or under-addressed by current care models. And COVID-19 is one of the most monumental challenges we face today.

On that March conference call, the CPHR team set out to survey community members to discern how they were being impacted by the crisis. They devised an online questionnaire that took only about 10 minutes to complete; the results would be anonymous, used for research purposes only. The questions pertained to health and employment status before and after the lockdown, how people were getting information about the disease spread, and similar queries.

By the time the survey closed one month later (by April 24), about 5,600 people from around the country had answered either all or most of the questions. While tabulating the results, the researchers were struck by one finding in particular: Respondents’ reported stress levels were alarmingly high.

An anxious nation

The CPHR team added to the survey several questions that draw from a screening tool for generalized anxiety disorder, called GAD-2. A GAD-2 score of 3 or higher is considered to be positive and often warrants either referral for consultation with a behavioral health provider or additional conversation and counseling with a primary care provider.
Pathway offered to women diagnosed with pre-eclampsia, propose potential solutions.

In this way, CPHR investigators are helping to alert the larger Health, the region and the nation on research projects stage at CPHR, many of the studies the investigators were concerned about burnout among the clinical staff, and they asked the CPHR team to survey System physicians. In all, 395 providers completed the survey, of which 70 percent had themselves tested positive for the virus, and 57 self-quarantined due to exposure. Nearly 40 percent of respondents reported moderate to severe symptoms of burnout, and more than half reported feeling a great deal of stress because of their work. “Health systems around the world are grappling with how to keep their workforce healthy during this outbreak,” noted Dr. Larson. “Main Line Health is keenly and actively focused on assisting its clinical staff through these difficult times.”

Inequitable care for all

While the COVID-related research has taken center stage at CPHR, many of the studies the investigators were pursuing before the crisis continue. Indeed, at any given time, the CPHR team is working with partners in Main Line Health, the region and the nation on research projects studying barriers to care and whose results can be used to propose potential solutions. For example, in its work with Main Line Health’s Women’s Heart Health program, CPHR researchers want to answer the question: What is the long-term care pathway offered to women diagnosed with pre-eclampsia, a high-risk disorder of pregnancy characterized by high blood pressure?

“African American women are particularly prone to this condition, and we know their pre-eclampsia makes them more likely to have cardiovascular problems later in life,” said Kyle McGregor, PhD, assistant professor and associate director of CPHR. “We want to find out if they’re being referred to a cardiologist, and if not, why?”

As part of its research, the CPHR team seeks to start a registry of these women so it can check in with them over a long period of time, as much as 10 to 15 years, to gauge their heart health. “Our goal is to set up a protocol that will help these women get the care they need in both the short and long term,” said Dr. McGregor.

Physician burnout studied

Another current project centers on bioethics, one of Dr. McGregor’s core research interests. Working with the Main Line Health Clinical Ethics Committee, he seeks to better understand issues that occur among clinicians, including physician burnout and moral injury, a hot topic in health care today. A pre-COVID national survey found 42 percent of physicians feel burned out from their workloads. While that number is down from 46 percent five years ago, it’s still too high by most health system standards. During the pandemic, Main Line Health administrators are concerned about burnout among the clinical staff, and they asked the CPHR team to survey System physicians. In all, 395 providers completed the survey, of which 70 percent had cared for at least one COVID-19 patient. Five providers had themselves tested positive for the virus, and 57 self-quarantined due to exposure.

The projects discussed above are only some of the many research projects ongoing by the CPHR team in their quest to advance patient care and health equity.

With CPHR in place, Main Line Health has furthered its quest to advance patient care and health equity. “With CPHR in place, Main Line Health has furthered its role as a thought leader in the field of community-based health care in America,” said Jack Lynch, FACHE, President and CEO of Main Line Health. “Dr. Larson and her team’s research oftentimes can be broadly generalizable for other health care systems across the nation to use to improve the well-being of their patient populations. Here at Main Line Health, we remain committed to care for our community and providing high-quality equitable health care for all.”

For more on the work of CPHR, visit mainlinehealth.org/cphr.

In addition to the COVID-19 research highlighted on previous pages, other LIMR investigators have turned their teams to fighting the pandemic.

Vaccine

LIMR Professor Ellen Heber-Katz, PhD, is focusing on her previous work on a generalized vaccine strategy that may prevent infections from any virus, including SARS-CoV-2. While at the Wistar Institute before coming to LIMR, she and a colleague developed a peptide-lipid-liposome compound as a potential vaccine for herpesvirus infection. In mice the compound showed a surprising result — no antibodies to the virus were created, but the animals had a powerful T cell response that protected them from a lethal viral dose. From this discovery the team learned that T cells alone can kill viruses and virally infected cells, thus leading to protection.

Intrigued by the unanticipated response to this agent, the team next tried the formulation on rabbies and found protection there, too. Again, no antibodies were created, but T cells appeared and were implicated in the protection seen. The team published several papers, but this direction eventually was discouraged given resistance from many experts then to the idea that a pure T cell response in the absence of antibodies could lead to protection against a viral disease. But, as always, times change.

“The world continues to search for vaccines for viruses, and the focus is on an antibody response. But there are cases where antibodies actually enhance the deleterious effect of viruses; this may be true for HIV and SARS and now COVID-19,” said Dr. Heber-Katz. “That’s the inherent problem with traditional vaccine development and is something we at LIMR are trying to resolve.”

Using her innovative vaccine approach she tested immune responses to an HIV analogue in primates, although protection studies weren’t carried out. Still, this was a first step to translation into the clinic. Recently, her team modified the original concept, hoping to test a novel, potentially stimulatory, adjuvant to the vaccine construct. The peptides they’ll use will be COVID-19 spike protein-derived.
Two LIMR Researchers Win Prestigious Awards

We are thrilled to report that Charles Antzelevitch, PhD, professor and executive director of cardiovascular research at LIMR, received the 2020 Lifetime Achievement Award from the American College of Cardiology (ACC), a non-profit medical association, for his groundbreaking research into abnormal heartbeat syndromes (arrhythmias). Dr. Antzelevitch, who also serves as director of research for Lankenau Heart Institute, has devoted much of his career to the study of the mechanisms underlying arrhythmias, including atrial fibrillation (AF) and inherited cardiac conditions. He and his colleagues also have contributed significantly to studies aimed at the development of new medications to treat AF.

During his 42-year career, Dr. Antzelevitch’s contributions to the scientific literature include more than 550 original papers and reviews, over 380 abstracts, and seven books. His research has been funded by the National Institutes of Health, the State of New York Department of Health, the New York Stem Cell Foundation, and the Women’s Board of Pennsylvania. During the next 25 years, Dr. Antzelevitch and his colleagues have contributed significantly to studies aimed at the development of new drugs to treat AF.

LIMR Assistant Professor Marie Webster, PhD, was the lead author of “Paradoxical role for wild-type p53 in driving therapy resistance in melanoma” in the prestigious journal Molecular Cell.

Advancing Patient Care Through Research and Physician Training

When Leonard Dreyfus, MD, Lankenau Medical Center’s former chief of cardiology, stopped down in 1989, Lankenau went searching for a department leader who could carry on his legacy in delivering world-class electrophysiology and cardiology services. Dr. Dreyfus was an influential leader whose highly regarded work in the field of cardiology included a term as president of the American College of Cardiology, so the bar for his successor was set high.

It was a sign of Lankenau’s great status and enormous good fortune to recruit Peter Kowey, MD, who brought an impressive global reputation in patient care, a commitment to research and a generous spirit, the breadth of which grew ever larger during his career here.

Dr. Kowey graduated from the University of Pennsylvania Medical School and trained in cardiology at the Peter Bent Brigham Hospital (now Brigham and Women’s Hospital) and the Harvard School of Public Health before spending nine years as an academic cardiologist at the Medical College of Pennsylvania. During the next 25 years, Dr. Kowey and his dedicated staff turned Lankenau into the internationally renowned heart-care hospital that it is today.

He has been a powerful influence not only at Lankenau and Main Line Health, but also in the field of cardiology around the world. I’ve been able to influence two generations of physicians: the generation I trained at the beginning of my career, and those more recently in training. Over the course of my career, I’ve trained thousands of fellows, residents and students, and taught legions of practicing physicians. Best of all, I continue to be active, helping with the fellowship program at Lankenau. I still see patients, much of the time with a fellow or student at my side.

Q: You’ve had a tremendous influence on an entire generation of cardiovascular specialists. Why is physician training a driving force in your work?

Dr. Kowey: When you train the next generation of doctors, it impacts patients everywhere. Our trainees are distributed around the world. I’ve been able to influence two generations of physicians: the generation I trained at the beginning of my career, and those more recently in training. Over the course of my career, I’ve trained thousands of fellows, residents and students, and taught legions of practicing physicians. Best of all, I continue to be active, helping with the fellowship program at Lankenau. I still see patients, much of the time with a fellow or student at my side.

Q: What is your most important piece of advice to your trainees?

Dr. Kowey: Your Own Device,” was published by iUniverse in March. I’ve penyved five medical mystery books. The fifth, “Death by Your Own Device,” was published by iUniverse in March. I’ve increasingly donated time to institutions I love. For example, I’m a member of the Board of Trustees at St. Joseph’s University. And I spend as much time as possible with my wife, who is my best friend and confidant, and my family. I have six grandchildren, ages 12 to 20, who live in Boston and California, so we have those as preferred travel destinations. I also stay physically active, hiking, skiing, cycling, and playing golf and tennis. 
LISA Program: Developing Impactful Research Collaborations

The Lankenau-Israel Strategic Alliance (LISA) fosters mutually beneficial cardiology research at Lankenau Medical Center, LIMR and Israeli institutions. Professor Charles Antzelevitch, PhD (left), consults in his LIMR lab with the most recent LISA fellow, Gilad Margolis, MD, of Tel Aviv Medical Center.

Many of the biomedical research advancements in recent decades have been the result of fruitful collaborations among investigators from different institutions, even from different parts of the world. The innovative research being done at Main Line Health is no exception.

The Lankenau-Israel Strategic Alliance (LISA) synthesizes synergic networks among physicians and scientists at Lankenau Medical Center, LIMR and Israeli institutions. Under the umbrella of the Israel Heart Society, this program, which began in 2017, fosters mutually beneficial cardiology research.

“Lankenau Medical Center is known worldwide for being a leader in cardiac care delivery and research,” said Charles Antzelevitch, PhD, professor and executive director of cardiology at LIMR. “With the LISA program, Lankenau is leading the way in cardiac research, collaborating with researchers at Israeli institutions.”

The initiative was developed by Dr. Antzelevitch; Peter Kowey, MD, a Lankenau-based cardiologist; Jeannie and Mark Cohen, and Dr. Michael Glikson, past president of the Israel Heart Society. The Cohens along with other generous donors, Lankenau Medical Center and the Israel Heart Society are enthusiastically funding the program.

The first LISA Fellow selected to participate was Ilat Weissberg, MD, PhD, an internal medicine resident at Israel-based Soroka Medical Center. He joined the Cardiovascular Research Program at LIMR in 2017 and served in that role until 2019. As a LISA Fellow, Dr. Weissberg participated in several ongoing projects at LIMR, including studies examining genetic defects in ion channels found in both the brain and heart and responsible for sudden unexpected death among epileptics.

Gilad Margolis, MD, from Tel Aviv Medical Center, served as the second LISA Fellow at Lankenau. He was selected to participate in the program by the Israel Heart Society via a nationwide competition.

He spent a year in a basic science training program at LIMR, working with Dr. Antzelevitch and his research team. Dr. Margolis participated in studies to determine why patients with cancer are prone to developing irregular heartbeats and how best to treat them. He also studied mechanisms that lead to inherited cardiovascular syndromes and therapies to prevent sudden cardiac death in these patients.

“Through LISA we are able to support important collaborations among the world-renowned clinicians at Lankenau Heart Institute, the researchers at LIMR and their esteemed colleagues in Israel,” said Mark Cohen, a member of Lankenau’s President’s Advisory Council. “The program sets the stage for an exciting exchange of ideas and best practices that can help improve cardiovascular research and patient care both here in the Philadelphia area and in Israel. I am thrilled to have been able to help launch this important program and am grateful to the other generous donors who have contributed to its resounding success.”

LISA Program Donors

We gratefully acknowledge the LISA program donors:

- Lisa and Arthur Berkowitz
- Jeannie and Mark Cohen
- Clayman Foundation/Mr. and Mrs. Stephen A. Cohen
- The Charlestein Foundation of Premier Dental Products Company
- The Daniel Veloric Foundation
- Mr. and Mrs. Bernard Zolot

“as of 2/28/20

If you would like to help ensure the future of this worthwhile program, contact Amy Mansky of the Lankenau Medical Center Foundation at 484.476.8070, or manskya@mlhs.org.

Your Investments in Research at LIMR Can Have a Significant Impact

You can designate a special fund to help precisely target your contributions to support what matters to you.

COVID-19 Research Fund

Your gift will support several biomedical scientists at LIMR who have pivoted their research toward battling the coronavirus. They are advancing studies to better diagnose, treat and prevent COVID-19 infection. Several LIMR Board Members have joined together to initiate a Challenge Match to help raise additional funds to support LIMR’s COVID-19 research. For the remainder of 2020, they will match dollar-for-dollar all contributions to this fund up to $80,000, thereby doubling your donation to this important research.

Immunotherapy Pioneer Fund

Immunotherapy entails the prevention or treatment of disease with substances that manage the immune system’s capabilities to clear disease, rather than attack the disease itself. LIMR has spearheaded unique studies of disease modifier pathways that impact immunity and cancer progression, developing new drugs to target them. Your generous contributions to this fund will help us to continue to advance these innovative directions.

Regenerative Medicine Vision Fund

Regenerative medicine deals with new processes of replacing, engineering or regenerating human tissues to restore or establish normal function. LIMR is privileged to have one of the pioneers in regenerative medicine, Professor Ellen Heber-Katz, PhD, who has discovered an experimental drug approach that may eliminate a need for stem cell transfer. Your contributions to the Regenerative Medicine Vision Fund will help further her research.

Biotechnology Innovation Fund

This fund supports work on biological molecules engineered by LIMR scientists that can enhance the diagnosis, prognosis and treatment of disease. Your generous contributions to this fund can help advance the work of our researchers including, for example, our studies on targeted nano-carrier therapeutics as experimental treatments for cancer, and our work on cloned human antibodies as treatments for infectious disease, cancer and neurological illnesses.

Cardiovascular Breakthrough Fund

Cardiovascular disease accounts for nearly 800,000 deaths in the United States every year, or about one of every three deaths. Additionally, about 92 million American adults are living with some form of heart disease or the after-effects of stroke. LIMR is home to world-renowned cardiovascular researchers. Your gift to this fund will further research that could benefit the lives of millions of heart disease and stroke patients.

LIMR Unrestricted Fund

Unrestricted gifts to LIMR are important in enabling opportunities to target your gift where our doctors and scientists believe it can have the greatest impact.

To donate to LIMR, please use the reply envelope inserted in this publication. You also can donate online at limr.org, and click on Supporters. Or call Amy Mansky of the Lankenau Medical Center Foundation at 484.476.8070, or email manskya@mlhs.org.
ABOUT MAIN LINE HEALTH

Main Line Health® is an integrated health system serving the Philadelphia region, with more than 2,000 physicians, one quaternary and three tertiary care hospitals, a wide network of patient care locations and community health centers, specialized facilities for rehabilitative medicine and drug and alcohol recovery, a home health service, and a biomedical research institute. Collectively, Main Line Health’s physicians, care teams, health care facilities, and researchers provide patients with primary through highly specialized care as well as access to clinical trials.