The Main Line Health clinical trials administered by LIMR offer patients access to potentially groundbreaking new devices and treatments for heart disease. 

Page 3

ALSO:

- Mastering Innovation and Impactful Population Health Research
- LIMR Discovery: A Protein That Plays Nice — Until It Doesn’t
- The Long-term Value of Investing in Research

Page 2
Page 7
Page 8
While we’re enormously proud of the Lankenau Institute for Medical Research’s 91-year history of breakthroughs in cancer research, it’s important to note that our investigators are advancing discoveries in many other conditions, most notably in heart disease. Today, our basic science researchers are uncovering the causes of heart disease and developing novel treatments that can help improve patients’ well-being and extend their lives.

That said, our work extends well beyond the laboratory. In fact, LIMR administers all of the cardiac clinical trials being conducted by the Lankenau Heart Institute of Main Line Health. During a clinical trial, researchers seek to determine, for example, how experimental medications, devices, and detection or diagnostic tools work in humans.

As you will read in our cover story beginning on page 3, Lankenau Medical Center has been leading and participating in many of the seminal heart disease-related clinical trials during the past four decades. In fact, the clinical research initiatives that led to the approval of almost all of the anti-arrhythmic medications and devices on the market today were either led by Lankenau clinicians or they participated in the research.

Over the years, Lankenau Medical Center has built an international reputation for its cardiac care, primarily in the treatment of structural heart diseases (SHD), conditions that typically involve the heart valves. And today, LIMR is administering numerous cardiovascular clinical trials, several of which seek to remedy SHD.

In this, our fifth edition of Catalyst magazine, you’ll read about the cardiac clinical trials program that is providing patients with access to the latest devices and treatment options for SHD. And you’ll learn more about the Structural Heart Team that, every day, is doing the vital work to improve the health of SHD patients and prolong their lives. I hope you will take a few moments to read about their work and the inspiring story of one of their patients.

In this issue, you also will read about LIMR’s discovery of a gene that increases the severity of disease in multiple chronic inflammatory conditions, such as rheumatoid arthritis, lupus and cancer. And we’ll take you behind the scenes to meet Robert Cox, PhD, LIMR’s director of scientific administration, who discusses LIMR’s infrastructure and equipment.

We hope you enjoy this issue of Catalyst. All of us at LIMR wish you and yours a Happy Holiday and a healthy and prosperous 2019.
Mastering Innovation and Impactful Research

The researchers found the variables that can predict readmission include older age, Medicaid insurance, discharge destination, severity of illness and a diagnosis of chronic obstructive pulmonary disease (COPD). The results can help staff reduce readmissions by tailoring interventions in the most efficient and cost-effective manner.

A follow-up study in 2017 took a deeper dive into the research to help uncover the predictors of avoidable emergency department (ED) visits at Main Line Health's hospitals and how to prevent unnecessary admissions from the ED. Previous research had shown ED visits increased since the enactment of the Affordable Care Act and Medicaid expansion, contributing to ED crowding in hospitals nationwide. There’s a continual concern that EDs are being used by some patients for non-urgent matters, which may hinder providing care to patients in truly urgent situations.

“We learned of several targeted interventions that could encourage or facilitate patients’ use of primary care services instead of the ED, especially for non-urgent and chronic conditions,” noted Sharon Larson, PhD, professor and executive director of the Main Line Health Center for Population Health Research at LIMR. “It was a valuable research report that offered actionable data to help improve our ED patient care.”

As Mr. Robinson added, “The research findings also helped to inform our design decisions for Lankenau’s new ED currently under construction. It helped us understand, for example, patient flow through the ED and how we can improve that.”

Main Line Health’s third CHOT research project will continue to focus, in part, on ED utilization. Said Mr. Robinson, “Our membership in CHOT shows our continued commitment to leadership in research and innovation, especially to expanding on our expertise in population health research.”

The 30 industry members of CHOT include not only Main Line Health and several health care systems in other parts of the country, but also technology companies, software providers, insurers and care-coordination ventures. They work with researchers at eight universities that are CHOT members, including Penn State, Texas A&M, and Georgia Tech.

“For industry members like Main Line Health, CHOT offers a space to interact with their peers in health care delivery and to affect and direct academic research on topics that are important to them so that the findings are most relevant to their organization,” said Bita Kash, PhD, MBA, CHOT center director.

Each year as a CHOT member Main Line Health gets assigned an academic researcher from a CHOT university site. Main Line Health joined the organization in 2011, and its first research project was led by a professor of health policy and management at Texas A&M. The project’s purpose was to identify factors associated with unplanned 30-day readmission rates at Main Line Health hospitals.

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Structural heart disease clinical trials

With the goal of helping patients live healthier and longer lives, Main Line Health conducts clinical trials that involve participants who are willing to help advance medicine into new frontiers. This partnership between patients and researchers can lead to a better understanding of how to diagnose, treat, and prevent certain diseases or conditions. If you’ve been diagnosed with a heart condition, talk with a cardiologist today or call 484.476.3030.

Clinical trials, which are administered by LIMR’s Center for Cardiovascular Clinical Research, are one of the critical treatment methods leading to FDA approval for new interventional cardiac and peripheral devices. “For some heart patients, research trials can offer an alternative solution to traditional treatments and in most cases, the use of a minimally invasive approach,” he said.

“Patients across Main Line Health are receptive to clinical trial participation,” said Dr. Goldman. “They know clinical trials offer access to devices and/or procedures that otherwise wouldn’t be available to them. In some cases, there literally are no other alternatives to get the newest devices.”

Dr. Gray added that, in many instances, Lankenau is the only site in the region where some trials are being conducted, which is why many patients travel great distances to participate. Moreover, Lankenau is the leading site for two national trials under the FDA’s novel Early Feasibility Studies (EFS) program, and is participating in a third EFS trial. EFS provides a way for innovators to work directly with trial sponsors, FDA review teams and clinicians to increase the efficiency of cardiac device development. The EFS program typically involves only a small number of trial centers at any given time — three to five nationally — so the fact that Lankenau is currently involved in three of them speaks highly to the clinical research team’s impressive track record.

Additional benefits of clinical research

While providing the most advanced care possible to patients will always be the number one priority, offering clinical trials has other benefits, too. “It builds our reputation, which helps facilitate the recruitment of top-notch physicians and our facility — from labs to the loading dock to the glass-wash facility, and everywhere in between. I try to anticipate needs and stay up to date with research protocols.”

Q: How would you define your role here at LIMR?

Dr. Cox: To stay in the forefront of medical research, we must replace scientific equipment on an ongoing basis. For example, we will soon need to replace several 40+ year-old freezers, and we need new biochemistry cabinets and centrifuges. We have one shaking incubator and could really use another. To identify and characterize the chemical structures of molecules, we would like our LIMR researchers to have a new mass spectrometer, which costs about $60,000. A relatively immediate need is an ultrasound machine for the animal facility, which costs about $120,000. We also have one functional incubator and could really use another.

To identify and characterize the chemical structures of molecules, we would like our LIMR researchers to have a new mass spectrometer, which costs about $60,000. A relatively immediate need is an ultrasound machine for the animal facility, which costs about $120,000. The machine we currently have will eventually be phased out, which means no spare parts currently are available.

That said, our immediate needs are in the range of $250,000 worth of scientific equipment.

Your donation can help purchase scientific equipment so that LIMR’s investigators can continue to advance biomedical research and improve patient health and well-being.

Q: What are LIMR’s greatest operational needs?

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Q: What would you define your role here at LIMR?

Dr. Cox: My job is to ensure continual operation of our research initiatives. I make sure that LIMR scientists have top-of-the-line equipment in the most modern labs and that everything is in perfect working order. Staying on top of infrastructure needs takes me into every nook and cranny of
**Updates From LIMR Researchers**

**Main Line Health Center for Population Health Research (CPHR) at LIMR produced a scientific review of supervised consumption facilities (SCFs) as a means to help combat the opioid epidemic. The study was produced by CPHR at the request of The Office of the Health Commissioner, Philadelphia Department of Public Health. SCFs are medical interventions in which essential services are provided to reduce substance use, the harms associated with substance abuse, and fatal overdoses. Sharon Larson, PhD, executive director of CPHR, was invited to give several talks around the city this year on her team’s research findings.

**Professor Jim Mullin, PhD, and a colleague from the University of Pennsylvania were awarded a grant from the National Institutes of Health (NIH) to study the effects of Ebola virus on the gastrointestinal tract.**

**Professor Charles Antzelevitch, PhD, and his team were awarded an NIH grant to study novel treatment approaches for the management of life-threatening cardiac arrhythmias.**

**LIMR researchers created a simple diagnostic test for an autoimmune disorder that can lead to serious psychiatric symptoms. They isolated and cloned auto-antibodies that may help elucidate the underlying cellular mechanisms of anti-NMDA receptor encephalitis, a type of brain inflammation. Scott Dessain, MD, PhD, the Joseph and Ray Gordon Chair in Clinical Oncology and Research, was the lead researcher on this groundbreaking study.**

**Associate Professor Laura Mandik-Nayak, PhD, was named to the Department of Defense’s Study Section for its new Lupus Research Program, part of the Congressionally Directed Medical Research Program.**

**LIMR President and CEO George Prendergast, PhD, gave the talk “Cancer and the Microbiome” at the 2018 Imagine Solutions Conference held in Naples, Florida, in February. He was invited by the American Cancer Society to give his talk, which was part of the conference’s National Cancer Summit.**

**Professor Ellen Heber-Katz, PhD, a world-renowned expert in regenerative medicine, was an invited guest of the director general of Science Foundation Ireland (SFI) to attend SFI’s St. Patrick’s Day Science Medal Awards and St. Patrick’s Day Global Ireland event in Washington, D.C., in March. The event was hosted by Dan Mulhall, Ireland’s ambassador to the U.S. in attendance was Ireland’s Prime Minister Leo Varadkar and Dr. France Cordova, director of U.S. National Science Foundation.**

**Dr. Susan Gilmour Named Deputy Director of LIMR**

Susan Gilmour, PhD, a professor on the resident faculty at LIMR, has been named LIMR’s new deputy director. Dr. Gilmour, who has been at LIMR since 1990, is a cancer researcher well known for her work on polyamines, a class of nutrients for which all cancers have a voracious appetite. Throughout her career, her overarching goal has been to translate her basic research findings into therapies that can contribute to increased survival in cancer patients.

Dr. Gilmour earned a bachelor’s degree in biology at the University of Virginia, her PhD in toxicology and pharmacology from Rutgers University/University of Medicine and Dentistry, followed by a postdoctoral fellowship in molecular carcinogenesis at The Wistar Institute in Philadelphia. For more than 26 years, her research has been supported by funding from the National Institutes of Health. She also has received multiple additional grants including those from the U.S. Department of Defense, Boehringer Ingelheim, W.W. Smith Charitable Trust, and Sharpe-Strumia Research Foundation.

**LIMR Launches New Website**

LIMR’s website, limr.org, underwent a complete redesign earlier this year. The new site offers:

- Descriptions of the more than 50 clinical trials ongoing at Main Line Health
- Answers to frequently asked questions about clinical studies
- Complete profiles of LIMR’s 18 resident faculty
- LIMR’s long and storied history and accomplishments through the past 91 years
- Our technologies invented, licensed or available for licensing
- Helpful information for those who would like to contribute to LIMR’s research advances, including profiles of four prominent contributors

Even complete past issues of this magazine, Catalyst, are available. Bookmark it today: limr.org.

**Discovery: A Protein That Plays Nice — Until It Doesn’t**

Researchers at LIMR uncovered a gene that increases the severity of disease in chronic inflammatory conditions, including rheumatoid arthritis, lupus, macular degeneration and cancer. Specifically, their studies showed the gene RhoB helps cells respond to certain stresses and will actually promote disease if those stresses are unresolved and thus become chronic in nature.

Think of RhoB like the quiet kid in the playground who typically helps maintain the peace with other children. But when continually provoked, that same child turns hostile and wreaks havoc on the group’s stability. You’re left wondering: “Wow, I didn’t realize how influential this child could be.”

“RhoB is not a crucial player in healthy states, but when stresses accumulate we’ve shown it’s very important in promoting a pathogenic immune response; that is, it’s capable of increasing the severity of diseases,” said Lisa Laury-Kleintop, PhD, LIMR associate professor. “RhoB acts as a stress-response mediator that influences the severity of inflammatory signals. It doesn’t seem to be involved usually in normal immunity. But in chronic immune states such as autoimmune disease it is critical for autoantibody production and inflammation. These features make RhoB a good subject to block as a general treatment for many autoimmune diseases and age-associated inflammatory diseases.”

**A key player in autoimmune disorders**

Autoimmune disorders and other chronic inflammatory diseases are skyrocketing in incidence globally. At LIMR, researchers seek to identify molecules that modify inflammatory severity in such diseases. In one important line of work, Dr. Laury-Kleintop has led preclinical studies demonstrating that blocking the RhoB protein can strongly blunt development of rheumatoid arthritis (RA), a debilitating joint disorder, and lupus, a disease caused when the immune system turns on the body and attacks its own tissues.

As published last year, LIMR researchers showed that laboratory mice bred to be without the RhoB gene had a markedly decreased incidence of arthritis and disease-causing autoantibodies. And when other mice developed arthritis and are given an anti-RhoB-targeted treatment, the disease subsides to a large extent. Interestingly, the treatment doesn’t appear to affect a normally functioning immune system — a stark contrast to all other treatments for autoimmune disease, which greatly increase risks of infection and other undesirable side effects.

“Our observations using two preclinical autoimmune models, RA and lupus, suggest a function for RhoB in specific autoantibody production of autoantibodies that contribute to autoimmune disease,” said Laura Mandik-Nayak, associate professor at LIMR and lead author of the study. “When we targeted RhoB with an antibody, we reduced the development of autoantibodies in both models. This was a surprising result, and we’re excited about its potential therapeutic implications.”

**Blocking blood vessel formation**

In addition to work on RhoB and autoimmune disorders, research has shown the benefit of blocking RhoB’s actions on other disorders, such as diabetic retinopathy and macular degeneration. “Our antibody against RhoB that arrests autoimmune disease also appears to inhibit the growth of abnormal blood vessels seen in the retinal disease ‘wet macular degeneration, which occurs often in the elderly,” explained Dr. Laury-Kleintop.

This line of work dovetails with studies of RhoB in cancer, pioneered in part at LIMR, where it was shown that RhoB is needed to drive formation of blood vessels that tumors need in order to grow. Furthering the connection between RhoB and diseases, Dr. Laury-Kleintop noted that levels of RhoB have been reported to rise naturally during aging and that high levels of RhoB are found in other inflammatory diseases, such as chronic kidney disease where it appears in the urine of patients, perhaps useful as a biomarker.

In keeping with a focus on translating findings in the lab into the clinic, LIMR developed and patented preclinical models that interact with RhoB and limit its function in preclinical models of diseases. “We’re working with a New England-based biotech company that we hope will license the technology and bring it to clinical trials,” noted Prendergast. “Through such a partnership, we seek to test the anti-RhoB therapy in autoimmune diseases like RA and lupus, or perhaps also in cancer or ocular disorders of the retina. We believe this unique agent to treat inflammatory diseases in a specific manner, leaving the normal immune system intact, has significant potential to improve patients’ lives and well-being.”

**Your donation can help advance the development of this therapy that has already demonstrated great potential and has the capacity to improve patients’ lives in the future.**
**The Long-term Value of Investing in Research**

In medicine, hope springs from research. At the Lankenau Institute for Medical Research (LIMR), this is our core precept. We know that nearly every life-saving medication, medical device and health care procedure used today by a clinician to help a patient started from a researcher’s experiment. Someone at some point had a new thought, “I wonder if this might work.” That’s the first step in improving medical practice — or as biomedical scientists say, in moving from bench to bedside.

Research not just time, creativity and great diligence. It also requires financial support. Your investments in research at LIMR can have a significant impact on health care. Our scientists are expanding the frontiers of human health, blending knowledge-based academic culture with invention-based entrepreneurship — our unique “acapreneurial” culture.

- In cancer research, our faculty focus on disease modifier genes and experimental drugs that influence inflammation and immunity. These drugs empower new types of immunotherapy with the capability to eradiclate metastatic disease. Our scientists are globally recognized for their expertise in tumor metabolism and immune modulation in the tumor microenvironment, putting LIMR at the forefront of the immunotherapy revolution in cancer. Our clinical researchers study the latest experimental therapies developed by pharmaceutical groups and the National Cancer Institute, including molecular targeted therapies that attack the specific needs in a patient’s specific tumor (also known as personalized medicine).
- In cardiovascular research, our faculty focus on new drugs and devices to correct abnormal heartbeat (arrhythmia), treat and prevent heart attacks and strokes, and avert heart failure. They also conduct bioengineering studies aimed at growing new hearts from a patient’s own cells. Our world-renowned clinical researchers conduct their studies at the Lankenau Heart Institute, one of the top-performing cardiovascular medicine and surgery centers in the country.
- In other areas, LIMR investigators use the knowledge they have created to devise new experimental treatments for arthritis, diabetes, lupus, infectious disease, neurological disorders and gastrointestinal disease. We also have international leaders in regenerative medicine and population health as part of our vision to create patient solutions of the future.

Every day our researchers seek to not only advance scientific discoveries in ways that can most rapidly impact health care, but also to train the next generation of researchers in ways that can most rapidly impact health care today, but to also train the next generation of scientists so that biomedical innovations can benefit the health of future generations of patients.

Today’s investment, tomorrow’s cures

The challenge we face is that the mechanisms that fund research activities in this country have changed dramatically. For decades most biomedical research funding came from the public sector, most notably the National Institutes of Health (NIH), an agency within the U.S. Department of Health and Human Services. Beginning around the turn of this century, the percentage of NIH applicants awarded grant funding has declined in real terms, as other pressures on federal entitlements and needs have increased.

To put our struggle into perspective, one important grant-funding mechanism from the NIH on which many biomedical investigators depend has significantly decreased over the past 20 years. Today, fewer than one-fifth of the scientists who apply for this support actually receive it.

As a result, biomedical researchers must secure funding alternatives in the private sector or abandon their research altogether. Who knows what future cures, medical devices and new standards of care will be left undeveloped simply due to lack of funding?

Through the ages, our nation has prided itself on its spirit of innovation and risk-taking, driven by the boundless energy and optimism of its people. In the biomedical arena, U.S. researchers account for over 75% of medical innovation worldwide. But this leadership is under great fiscal pressure. If, like me, you believe in the inherent value of the foundational attributes of research needed to drive innovation, I encourage you to target your gift where our doctors and scientists believe it could have the greatest impact.

To donate to LIMR, please use the reply envelope inserted in this publication. You also can donate online at www.limr.org, and click on Supporters. Or call Rebekah Sassi, executive director of the Lankenau Medical Center Foundation, at 484.476.8067 or email sassa@mlhs.org.

**Your Investments in Research at LIMR Can Have a Significant Impact**

You can designate one of the Lankenau Institute for Medical Research’s special funds to help precisely target your contributions to health care research that matters to you.

**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 attacking 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, enabling her and her team to continue groundbreaking work on this approach that holds enormous promise for the future of health care.

**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 could have the greatest impact.

In our Spring-Summer 2018 edition of Catalyst magazine, we published a story about the Gordon family (from left): Scott, Ray, Joseph, Leila and Hunter. We apologize for inadvertently omitting Hunter Gordon.
THE POWER OF GIVING

Charitable giving does not require great wealth, only generosity of spirit and a desire to share what one has for the benefit of others.

A gift to Main Line Health’s Lankenau Institute for Medical Research (LIMR) has the potential to do great good. LIMR’s ultimate mission is to prevent disease and reduce suffering. Your support makes this possible.

To learn more, visit mainlinehealth.org/LMCGiving or call 484.476.8070.

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.