

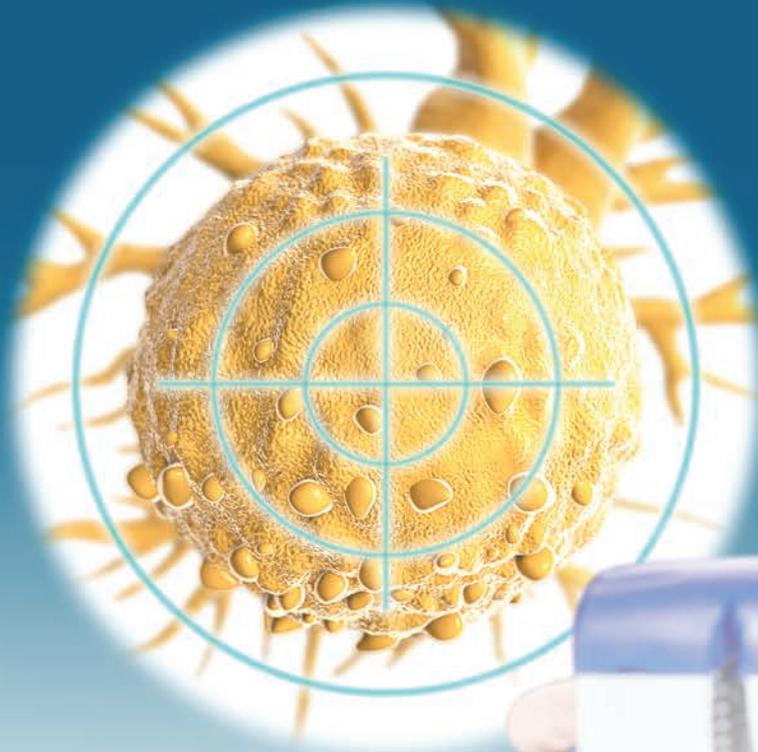


Main Line Health®

LANKENAU INSTITUTE FOR MEDICAL RESEARCH

# CATALYST

SPRING 2021



## IMPROVING IMMUNOTHERAPIES

Advancing the 21st century science of harnessing the immune system to kill cancer cells. | **Pages 3 & 4**

ALSO:

**Cardiogenetics: Helping Patients Make Informed Decisions About Care**

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**Paths Forged in Cardiac Research and Patient Care**

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**Turning Lab Findings into Approved Therapies**

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### About Lankenau Institute for Medical Research (LIMR)

LIMR is a nonprofit biomedical research institute located on the campus of Lankenau Medical Center and is part of Main Line Health. Founded in 1927, LIMR's mission is to improve human health and well-being. Faculty and staff are devoted to advancing innovative new approaches to formidable medical challenges, including cancer, cardiovascular disease, gastrointestinal disorders, autoimmune diseases, and regenerative medicine, as well as population health. LIMR's principal investigators conduct basic, preclinical and translational research, using their findings to explore ways to improve disease detection, diagnosis, treatment and prevention. They are committed to extending the boundaries of human health through technology transfer and training of the next generation of scientists and physicians. For more information, visit [limr.org](http://limr.org).

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**George C. Prendergast, PhD**

*The Havens Chair for Biomedical Research*

*President and CEO*

*Lankenau Institute for Medical Research,  
Main Line Health*

## WITH DEEP GRATITUDE

As I write this letter, I am feeling thankful for the vaccine developers around the globe and their extraordinary achievements in rolling out a safe and effective COVID-19 inoculation in record time, and to those who are distributing, administering and taking the vaccine. While the past year posed many challenges, we also witnessed a miracle of science within months of the pandemic's start, even though many people doubted a safe and effective vaccine could be produced so quickly.

In this spirit, I am grateful to our visionary donors who contributed more than \$265,000 to LIMR's COVID-19 Research Fund. They believed in the ability of our faculty to pivot rapidly to develop antibodies for use as national standards for infection testing by other scientists, explore backup vaccine designs, research novel treatments, and administer clinical trials. They are working collaboratively with researchers around the country, and I'm proud to report that their advances have helped inform the larger scientific community.

Along with others, I have termed the coronavirus vaccines and therapies developed this past year miracles. Certainly, their positive effects are wondrous, but the work that led us out of the pandemic's dark tunnel was not divine intervention. Rather, the work was done by highly trained scientists working together with diligence, urgency and a singular purpose. As we've said at LIMR over the past year: The path out of the pandemic runs straight through the biomedical laboratory.

Still, we have lost way too many souls to this virus, and if you have lost a loved one, I offer my sincerest condolences. I am confident we are stemming the infection's spread and learning lessons that will help thwart future pandemics.

If you contributed to LIMR's COVID-19 Research Fund — or any other LIMR initiative — you have my heartfelt thanks. Please know that your contributions have an enormous and positive impact on scientific discovery.

While our research on the coronavirus will continue as long as is needed, we also haven't lost our focus on other important projects. In this, our 10th edition of *Catalyst* magazine, you'll read about two LIMR investigators' work on

improving immunotherapies for cancer patients who either do not respond to other treatments or who eventually experience disease progression (see page 3).

You'll also read about the Main Line Health Cardiovascular Genetics and Risk Assessment Program that's giving patients with a personal or family history of cardiovascular disease access to more personalized information about genetic risks (page 2).

You'll meet two important investigators. Basel Ramlawi, MD, chief of cardiac surgery at Main Line Health, is a prodigious researcher of new cardiovascular devices and procedures (page 5). Melvin Reichman, PhD, senior investigator at LIMR and our chief science officer for small molecule therapies, is our resident expert on pharmaceutical development (page 7).

On a side note: Dr. Reichman organizes, in coordination with Lankenau's Annenberg Center for Medical Education, the Dynamic Duo seminar series. Given by LIMR investigators and clinical partners, the quarterly seminars (currently presented virtually) accelerate advances in patient care by fostering earlier collaboration between clinical and preclinical investigators. They also promote opportunities for basic research internships at LIMR to medical residents. I am grateful to Dr. Reichman for taking a leading role in this important initiative.

I hope you enjoy this edition of *Catalyst*. ✨

Please join us on Tuesday, April 27 at 7:00 pm for the webinar: "Are we nearing the end of cancer?" I will moderate a discussion among LIMR's cancer researchers Susan Gilmour, PhD; Alex Muller, PhD; U. Margaretha Wallon, PhD; and Marie Webster, PhD. See the back cover for details.

## Cardiogenetics Program Helps Patients Make Informed Decisions About Care

**Y**ou may know some cancers can be inherited, but did you also know that certain cardiac conditions can, too? These include arrhythmias, cardiomyopathies, diseases of the aorta, and elevated cholesterol levels, any of which can be life-threatening.

Several LIMR investigators focus their research on inherited cardiac diseases — and are renowned for their discoveries. For example, LIMR Distinguished Emeritus Professor Charles Antzelevitch, PhD, and Professor Gan-Xin Yan, MD, PhD, led a global task force to develop the seminal report on J wave syndromes, inherited conditions that can lead to sudden cardiac death in young adults and sudden infant death syndrome.

Their expert report received endorsements from heart care associations around the world and was published simultaneously in three prestigious journals. Additionally, Drs. Antzelevitch and Yan coauthored a textbook on J wave syndromes.

### Determine genetic risk

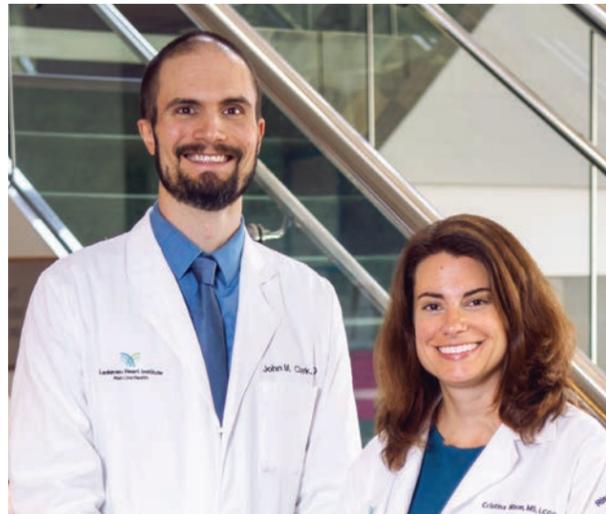
To extend this knowledge from the research lab into everyday life, the Main Line Health Cardiovascular Genetics and Risk Assessment Program was launched in 2019. The program provides patients who have a personal or family history of cardiovascular disease access to information about genetic risks.

Testing can identify more than 200 genes associated with cardiovascular conditions. For families with this genetic makeup, many opportunities exist to guide care and improve outcomes, advancing the exceptional cardiac services offered by Main Line Health and the Lankenau Heart Institute. Anyone concerned about cardiovascular risk due to a personal or family history can be seen by genetics experts in the program. Evaluation includes:

- an overview of cardiovascular risk factors and analysis of personal and family history;
- discussion of the likelihood of inherited disease risk;
- coordination of genetic testing (when indicated);
- interpretation of the results; and
- review of risk-management recommendations.

Supportive and informational resources are offered to patients when genetic risk for disease is discovered.

“Genetic counseling helps people review the pros and cons of genetic testing and the many emotions surrounding inherited cardiovascular risk to determine which testing strategy is best for them,” noted Cristina Nixon, MS, a licensed certified genetic counselor for the program.



John M. Clark, DO, medical director of the Main Line Health Cardiovascular Genetics and Risk Assessment Program; and Cristina Nixon, MS, licensed certified genetic counselor. (Photo was taken before social-distancing guidelines were in place.)

### Research registry

The clinical Cardiovascular Genetics and Risk Assessment Program also promotes further research initiatives. The development of a cardiovascular research registry will allow researchers to:

- study DNA variations and other biomarkers within de-identified patients and families at hereditary cardiovascular risk;
- pursue subsequent investigations aimed at earlier diagnosis, improved treatment or interventional management; and
- evaluate environmental trends related to heart conditions within the setting of inherited risk.

Initiation of the registry has been supported by a generous donation from Beth and Richard Probinsky.

“We’re pleased to offer this important clinical health service, as well as opportunities for research participation, to our heart care patients and their family members,” said John M. Clark, DO, medical director of the program. “Knowledge of genetic risk for cardiac disorders helps patients and health care providers better understand and manage cardiovascular disease now and in the future.”

For more on the program, call 484-565-GENE (4363), or visit [Mainlinehealth.org/cardiogenetics](http://Mainlinehealth.org/cardiogenetics). ★



Alex Muller, PhD, LIMR associate professor, and his collaborators developed a new cancer vaccine approach that shows significant promise in boosting the effectiveness of FDA-approved checkpoint inhibitor immunotherapies.

## Improving Immunotherapies

LIMR CONTINUES TO ADVANCE THE 21ST CENTURY SCIENCE OF HARNESSING THE IMMUNE SYSTEM TO FIGHT CANCER.

**D**uring the past two decades, LIMR researchers have been at the forefront of investigations on how to engage the power of the immune system in the fight against cancer. Their research has helped usher in the modern era of FDA-approved immunotherapies known as immune checkpoint inhibitors. These new treatments can provide long-term survival for some cancer patients previously considered incurable.

Despite these remarkable outcomes, there is still much work to do, as the current treatments remain inadequate for most cancer patients who either do not respond or eventually experience disease progression. That’s why LIMR researchers have redoubled their efforts to improve outcomes for cancer patients receiving immunotherapy.

Results of two recent studies conducted by LIMR investigators and their collaborators show significant promise in resolving these patient-care challenges.

### Cancer vaccine

In one preclinical study, subjects treated with an experimental cancer vaccine in combination with checkpoint inhibitor immunotherapy not only had total remission of their cancers, but even more encouragingly, also showed complete protection against re-introduction of tumor cells. In short, the study offered preclinical proof of concept for a completely new type of cancer vaccine approach.

This work, conducted by LIMR investigators in collaboration with Copenhagen-based IO Biotech, was designed to attack cells expressing IDO1, an enzyme that LIMR scientists discovered limits the cancer-fighting activity of chemotherapy by thwarting the immune system’s ability to eradicate tumors.

IDO1 is an unconventional candidate for vaccine-directed attack because it’s a normal “host” protein that, according to the textbooks, should be ignored by the immune system. But earlier work by LIMR’s collaborators at IO Biotech uncovered the presence of IDO1-reactive immune cells in patients. This finding fostered the idea that stimulating IDO1-reactive immune cells with a vaccine could result in effective anti-tumor immune responses — an idea now validated by the current study.

Several peptides (i.e., short stretches of amino acids from the entire IDO1 protein) were evaluated. Peptides activating different aspects of the immune response against IDO1 — referred to as class I-directed and class II-directed — were both shown in animal studies to have some intriguing anti-tumor activity.

Then, based on microscopic analysis of the tumors, the investigators combined the peptides with an anti-PD1 antibody, the latter of which is one of a class of immunotherapies that includes the FDA-approved drugs Opdivo® (nivolumab) and Keytruda® (pembrolizumab).



Susan Gilmour, PhD, LIMR deputy director, and her team developed a therapeutic shown to enhance the efficacy of today's cancer immunotherapies in patients whose tumors have become resistant to treatment.

The result? Much better responses than could be achieved with the individual treatments, including complete elimination of some tumors.

That wasn't all. The animals that responded to the combination treatment showed durable resistance to subsequent re-introduction of tumor cells.

This finding was important because it indicated that the immune system was activated properly to prevent relapse.

The promising results didn't stop there. The researchers found this immunological resistance could be transferred to a naïve tumor-bearing animal simply by transplanting immune cells from a therapy-treated subject to an untreated subject. The researchers credited this effect to the treatment regimen's ability to induce T-cells, a component of the immune system critical for stopping cancer growth.

"Identifying interventional strategies — such as this groundbreaking vaccine approach — that can overcome the limitations of immune checkpoint inhibitors given alone, and unleash the immune system to fight cancer in both the short and long term, is clearly of the utmost importance," said Alexander Muller, PhD, associate professor at LIMR, one of the study's authors. "These results were very encouraging."

The research, which was published in *Journal for ImmunoTherapy of Cancer*, was funded by IO Biotech, with additional laboratory support through the Lankenau Medical Center Foundation and Main Line Health.

LIMR's proof of concept for this groundbreaking vaccine approach to inactivate IDO1 in cancer is now being evaluated in clinical trials in combination with Keytruda® treatment. The very promising findings in early clinical trials led the FDA to designate the IDO1 vaccine a "breakthrough therapy." Accordingly, LIMR's pioneering work on IDO1-blocking therapies continues to advance in diverse directions.

#### Polyamine blockade

In another study, LIMR researchers found compounds that inhibit the actions of polyamines (small molecules that are essential for cell growth and proliferation) may enhance the therapeutic response and long-term survival of patients on cancer immunotherapies.

Cancers have a voracious appetite for polyamines, the levels of which are dramatically increased in tumors. LIMR investigators developed a polyamine blocking therapy

(PBT) consisting of an FDA-approved compound that stops polyamine biosynthesis and a novel transport inhibitor that blocks polyamine uptake into tumors. Unexpectedly, the researchers found that in animal models of metastatic breast cancer and melanoma, PBT activated the immune system to fight the cancers.

Based on that finding, they wondered if combining PBT with an immunotherapy could safely boost its efficacy, especially in settings where immunotherapy was ineffective on its own. In animals with tumors resistant to anti-PD1 immunotherapy, the researchers found that, while treatment with PBT alone reduced tumor growth, administering it with anti-PD-1 immunotherapy markedly increased its efficacy and significantly increased subjects' long-term survival.

The researchers noted that the study highlights the ability of PBT treatment to reinvigorate the T-cell-directed activity of immune checkpoint blockade and promote the immune system's ability to kill tumor cells.

"We showed that PBT can enhance the anti-tumor efficacy of immune checkpoint inhibitors such as anti-PD1 immunotherapy, increase the number of tumor-specific cytotoxic T-cells, and improve the survival of tumor-bearing mice," said Susan Gilmour, PhD, professor and deputy director of LIMR, and one of the study's authors. "This was an exciting finding because it shows that co-treatment with PBT may improve the efficacy of today's immunotherapies in patients with drug-resistant tumors that don't respond to anti-PD1, which has become the benchmark immunotherapy for treating a growing number of cancers."

For their study, which was published in the journal *Molecular Cancer Therapeutics*, LIMR researchers collaborated with a colleague at the University of Central Florida College of Medicine. The research was supported by grants from the U.S. Department of Defense, the National Institutes of Health, Lankenau's John B. Deaver Auxiliary, and Biostrategy Partners.

"With these studies, LIMR continues to advance the 21st century science of harnessing the immune system to fight cancer," said Dr. George Prendergast. "The highly intriguing results of this research point a path forward in leveraging strategies to treat cancer patients whose tumors are or have become resistant to what is increasingly being recognized as standard-of-care immune checkpoint therapies like anti-PD1." ✨

Want to learn more about the research of Drs. Muller and Gilmour? Tune in on April 27 for the webinar: "Are we nearing the end of cancer?" See the back cover for details.

## Forging Paths in Cardiac Research and Patient Care



Basel Ramlawi, MD, Chief of Cardiac Surgery, Main Line Health; Co-Director, Lankenau Heart Institute; and Clinical Professor, LIMR

A nationally recognized cardiac surgeon, Basel Ramlawi, MD, is a researcher and leader in minimally invasive surgical and transcatheter approaches to complex valve and aortic diseases.

Before joining Main Line Health in 2020, Dr. Ramlawi served as chair of the Heart and Vascular Center and founding director of the Advanced Valve and Aortic program at Valley Health, a six-hospital integrated health system based in Virginia. Prior to

that he served as an associate professor of surgery at Houston Methodist DeBakey Heart and Vascular Center, where he was co-director of the Aortic Surgery program and surgical director of the Atrial Fibrillation Management program. He earned his medical degree at McMaster University Medical Center in Canada, with postgraduate training at Columbia and Harvard.

Dr. Ramlawi is co-director of the Lankenau Heart Institute with William Gray, MD, and his research there is supported and administered through his faculty appointment at LIMR. His research interests include aortic diseases, valvular disorders, cardiac rhythm disorders and cardiac tumors.

**Q: Your clinical expertise is renowned. What compels you to also turn your attention to research?**

**Dr. Ramlawi:** Research was an integral part of my medical education, and since then I've been focused on it. I believe research makes me a better clinician and educator. I like building my expertise and then incorporating that knowledge into my practice for the betterment of my patients. A focus on research enables me to find newer, better ways to approach problems — approaches that may lead to improved outcomes and help patients in a less-invasive manner.

Evolution in medicine is inevitable, and I like being one of the people forging those paths and leading the way.

**Q: How have your research findings advanced your ability to offer high-quality patient care?**

**Dr. Ramlawi:** As a surgeon, I want to offer the very best care to my patients, and that can entail offering the latest technology available anywhere in the world. To do that, I often focus on research involving innovative new solutions, which means that, when appropriate, we can offer patients access to early-phase clinical trials of devices and techniques. That, in turn, puts us ahead of the curve in patient care — really, best-in-class care.

Then once those devices and techniques are FDA-approved, we've already been using them, perfecting our practice with them, so we can then teach other health care professionals. That's a big benefit to our patients who gain access to the very latest innovations in care and clinical expertise.

**Q: In which type of clinical trials are you involved?**

**Dr. Ramlawi:** I've been the principal investigator on several national studies, primarily those focused on transcatheter valve procedures and valve repairs, aortic aneurysms and dissections, as well as trials for new treatments for patients diagnosed with atrial fibrillation and at risk for stroke.

**Q: When you're able to carve out some free time, how do you like to spend it?**

**Dr. Ramlawi:** We have three children: two girls and a boy. Pre-pandemic, my family and I loved to travel. Our favorite destinations have been in Europe. I'm also an avid cyclist, which keeps my heart in good condition. ✨

For more on Main Line Health's cardiovascular clinical trials, visit [mainlinehealth.org/cardiacclinicaltrials](https://mainlinehealth.org/cardiacclinicaltrials)

## Updates from LIMR Researchers

Professor **James Mullin**, PhD, and two collaborators were awarded grants from Fast Grants for their COVID-19 research. Fast Grants is supported by several groups and individuals, including The Chan Zuckerberg Initiative (co-founded by Facebook founder Mark Zuckerberg); Elon Musk; and LinkedIn co-founder Reid Hoffman.

Assistant Professor **Marie Webster**, PhD, was awarded a grant from the W.W. Smith Charitable Trust for her proposal to determine the mechanisms of action that cause drug resistance in metastatic melanoma treatments.

Associate Professor **Laura Mandik-Nayak**, PhD, was awarded a grant from the Giorgi Family Foundation for her proposal to define the role of the enzyme IDO2 — discovered at LIMR — as a novel therapeutic target for rheumatoid arthritis.

Professor **Sharon Larson**, PhD, executive director of the Main Line Health Center for Population Health Research at LIMR, was named Chair of the Healthy Pennsylvania Partnership Executive Committee, which provides guidance for the State Health Assessment and the State Health Improvement Plan for the Pennsylvania Department of Health.

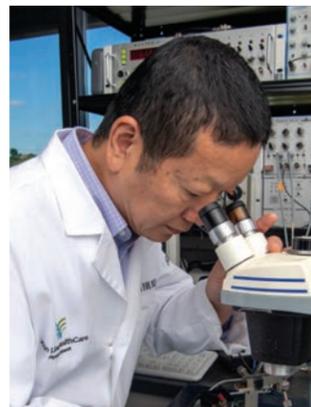
Professor **Peter Kowey**, MD, is ranked 20th in the U.S. among scholars writing about atrial fibrillation, according to Expertscape.

Research Associate Professor **Sunil Thomas**, PhD, was selected as a reviewer for SARS-CoV-2 and COVID-19 grant proposals submitted to the NIH's National Institute of Allergy and Infectious Diseases.

Research Professor **Hector Barajas-Martinez**, PhD, and Distinguished Professor Emeritus **Charles Antzelevitch**, PhD, published their findings that three genetic mutations cause the inherited cardiac disorders Brugada syndrome and Early Repolarization syndrome. The manuscript was published in the journal *Stem Cells International*.

Telesis Therapeutics, a company that licensed for clinical development the small molecule cancer drug TTL-315 discovered at LIMR, signed a collaborative research and development agreement with the National Cancer Institute's Frederick National Laboratory for Cancer Research.

## Serious Drug-Induced Side Effect Detected, Scored by LIMR Researcher



A new study coauthored by LIMR investigators showed the utility of a scoring system enabled by a LIMR-developed assay in predicting drug-induced torsade de pointes (TdP), a life-threatening cardiac condition.

TdP occurs in the setting of QT prolongation, an electrical disturbance in the heart. Clinicians have known that certain approved and

experimental medications can inadvertently cause QT prolongation. In fact, the U.S. Food and Drug Administration (FDA) now requires all drug candidates in development for treatment of any disease to be tested to ensure they don't cause QT prolongation before being approved for clinical use. But testing in patients isn't always ideal or feasible. So the FDA called for scientists to create preclinical testing methods that reliably and accurately predict the likelihood of a clinical effect.

LIMR Professor Gan-Xin Yan, MD, PhD (*pictured*) — along with colleagues at the FDA, Janssen Pharmaceuticals, GlaxoSmithKline and Peking University — demonstrated in a recently published, blinded study that their Normalized TdP Score System successfully predicted the proarrhythmic risk of 34 different medications.

To complete the study, the team used Dr. Yan's "wedge prep," an arterially perfused ventricular wedge preparation for heart tissue created in a petri dish. Using this invention one can accurately record all of the electrical signals in the heart, even in its innermost layers. Previously, scientists could record only the signals sensed on the outside of the heart, missing inner signals that are crucial for coordinating normal pump function.

In their work, Dr. Yan's wedge prep detected signals in the heart tissue, which had been treated with each one of the 34 studied medications. They then assigned scores to those drugs, thus enabling an accurate risk assessment of a medication's ability to induce TdP, as detected in the tissue preparation.

"There has long been a need to reliably predict TdP risk among drug candidates," said Dr. Yan. "We've now shown that using our normalized TdP score by the wedge prep assay can enable pharmaceutical researchers to readily determine drug-induced TdP risk among their compounds. We believe it has the potential to become a best-practice preclinical drug-safety solution for pharmaceutical development — perhaps even reducing the need for human QT studies."

This seminal study was published in the journal *Clinical Pharmacology and Therapeutics*. ★

## Turning Lab Findings into Approved Therapies



Melvin Reichman, PhD, director of the LIMR Chemical Genomics Center.

In meetings of LIMR scientists where investigators present their latest findings, George Prendergast usually asks the "why" questions: "Why did you conduct that experiment? Why are your discoveries important to science or medicine?"

Senior investigator Melvin Reichman, PhD, is often the first to ask the "how" questions: "How did you design the experiment and the controls? How do your findings extend your

prior data? How will your findings affect development of new medicines or products or their uses to improve patient care?"

A wide range of insightful queries like those help to ensure that LIMR's focus on the acapreneurial approach — a mix of academic culture with invention-based entrepreneurialism — stays top-of-mind among investigators.

Dr. Reichman, director of the LIMR Chemical Genomics Center (LCGC) and the institute's chief science officer for small molecule therapies, is LIMR's resident expert on pharmaceutical development, having directed drug discovery at five pharmaceutical companies before joining the institute in 2006. During his pharmaceutical firm tenure, he participated in the discovery of the blockbuster anti-inflammatory drug Celebrex®, the bone marrow stimulant Promacta®, and dozens of other medicines.

"One can do no greater good in science than helping cure a disease. That's why many of us became scientists," said Dr. Reichman. "Some small molecules literally become miracles as drugs to treat disease."

### Neurosciences

Dr. Reichman's path to a career in drug development started as an undergraduate at Brooklyn College. He used his dual major in psychology and chemistry to construct his own neurosciences program, with an emphasis on biochemistry of the brain. He then went on to study neurosciences at the University of Rochester School of Medicine-Center for Brain Research, where he was awarded his PhD.

While working for pharmaceutical companies, he directed high-throughput screening (HTS) operations. HTS allows automated testing of hundreds of thousands of

chemical and/or biological compounds for a specific molecular target, thereby accelerating new lead discovery in a cost-effective manner. He said his years in pharma gave him an eye for promising molecules.

"Only about 1 percent of initiated drug-discovery programs end up with an FDA-approved medication," explained Dr. Reichman. "Given the poor odds of success for any individual program, I devoted myself to HTS to help investigators better identify drug leads."

### LIMR Chemical Genomics Center

While at DuPont Pharmaceuticals, Dr. Reichman took his drive for drug development time- and cost-efficiencies a step further and designed the concept for a robot in which compounds, stored frozen, could be swiftly combined and screened for possible therapeutic efficacy. He built the now-patented machine, the NanoTube Repository System (NARS), at LIMR where it is housed in a cavernous room on the institute's ground floor. The state-of-the-art system's extensive chemical library of over 250,000 small molecules is suitable for HTS campaigns for the most challenging disorders, including drug-resistant infections and metastatic cancer.

"There's no system like this in any academic setting," said Dr. Reichman. "The NARS, together with the unique chemical collections we've amassed at LIMR and the special HTS methods we perfected, serve as unique resources to LIMR and drug-discovery scientists worldwide. Our materials and methods have supported several dozen projects that have resulted in peer-reviewed publications and advanced scientific understanding of disease mechanisms."

NARS is one of many offerings of LCGC, a division of LIMR that provides technology, specialized research services and resources to pharmaceutical developers in academia and industry.

For Dr. Reichman, the coronavirus pandemic has only hastened his efforts to improve patient care. Part of an international consortium to find new combination-drug treatments for COVID-19, he is designing experiments to identify antiviral compounds that work well with remdesivir, a drug used to treat COVID-related conditions. He also is working with a pharmaceutical firm to study a treatment for "cytokine storms," the dangerous immune reactions in COVID-19 patients that are responsible for most of the deaths the infection causes.

"Dr. Reichman's enormous expertise and insights on the regulatory aspects of drug development have been extremely valuable assets for LIMR as we continue on our mission to advance health and wellness among our patient populations," said Dr. George Prendergast. "We are fortunate to have him as a colleague." ★

## Hope Springs from Research



Kaylend Manley, biomedical research assistant, confers with LIMR Associate Professor Lisa Laury-Kleintop, PhD, who seeks to understand the development of cardiovascular, autoimmune, ocular and kidney diseases. (Photo was taken before social-distancing guidelines were in place.)

In a research lab, a scientist takes an experimental immunotherapy he developed, drips it into a petri dish of cancer cells mixed with immune cells, and peers into a microscope to study the reaction. In another lab, a world-renowned cardiovascular researcher and his team edit a manuscript announcing their much-anticipated findings on the mechanisms that drive inherited cardiac diseases. Upstairs in the vivarium, a regenerative medicine researcher checks the health of mice that were treated with her lab's newest innovation, a drug that may regrow limbs.

This is a day in the life of the Lankenau Institute for Medical Research (LIMR). This gem within Main Line Health has been at the leading edge of scientific discoveries since its founding in 1927. LIMR's principal investigators conduct basic, clinical, translational and population health research seeking to improve disease detection, diagnosis, treatment and prevention. Its resident faculty members conduct lab-based research on cancer; cardiovascular, autoimmune and gastrointestinal diseases; and regenerative medicine.

Additionally, LIMR's Clinical Research Center administers the approximately 100 clinical trials ongoing at Main Line Health, including trials for cancer, heart disease and COVID-19. And the Main Line Health Center for Population Health Research at LIMR serves as a research and educational partner to the System, informing and assessing initiatives to improve the health status and quality of life in the communities we serve.

### A storied history

Founded as one of the first cancer research centers in the nation, LIMR today is at the leading edge of the immunotherapy revolution in health care with the discovery and development of a new class of drugs called IDO inhibitors. Over the decades, LIMR investigators and their collaborators:

- discovered a genetic abnormality in cancer, the Philadelphia chromosome, a finding that heralded today's genetics revolution in oncology;
- identified the hepatitis B virus and developed a diagnostic test and vaccine — work that was awarded the 1976 Nobel Prize in Physiology or Medicine; and
- led or were actively involved in seminal clinical trials of almost all of the anti-arrhythmia drugs and devices prescribed and implanted by cardiac physicians today.

"LIMR has a rich history of health care innovations, and we continue to invent and patent our discoveries and run clinical trials," explained Dr. George Prendergast. In recent years, several biomedical start-up companies have been incubated at LIMR, more than 50 patents have been issued or are pending, and many LIMR-patented inventions have been licensed.

### Training the next generation

A mainstay of LIMR's mission is education. Medical and surgical residents and specialty fellows perform rotations at LIMR, thus gaining a deeper understanding of the science underlying treatments and clinical practices. The rotations also help enable the continued accreditation of Main Line Health's graduate medical education programs, for which research is a required element.

In short, LIMR advances patient health and well-being through research, rapidly transfers new technology to the bedside, and helps to train scientists and physicians. Said Jack Lynch, Main Line Health's president and CEO, "The work done at LIMR fuels the promise of a healthier tomorrow and serves as a critical component in Main Line Health's mission to improve the lives of all we serve."

To support LIMR and its mission, visit [limr.org](http://limr.org). ✨

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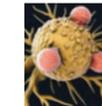
## Your Investments in Research at LIMR Can Have a Significant Impact

You can designate one of the following funds to direct your contributions and support research that is important 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.



### 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.



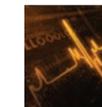
### Regenerative Medicine Vision Fund

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.



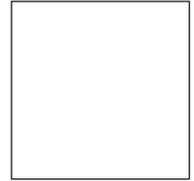
### Cardiovascular Breakthrough Fund

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 enable opportunities to target your gift where our doctors and scientists believe it can have the greatest impact.

To make a donation, please use the reply envelope inserted in this publication, or donate online at [limr.org](http://limr.org) (click on Supporters). Or call Amy Mansky of the Lankenau Medical Center Foundation at 484.476.8070, or email [manskya@mlhs.org](mailto:manskya@mlhs.org).



Speakers: Lankenau Institute for  
Medical Research Cancer Specialists



Susan Gilmour, PhD  
Deputy Director



Alex Muller, PhD  
Associate Professor



Marie Webster, PhD  
Assistant Professor



U. Margaretha Wallon,  
PhD, Assistant Professor



*Moderator:*  
George Prendergast, PhD,  
President & CEO, LIMR

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