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LANKENAU INSTITUTE FOR MEDICAL RESEARCH

CATALYST

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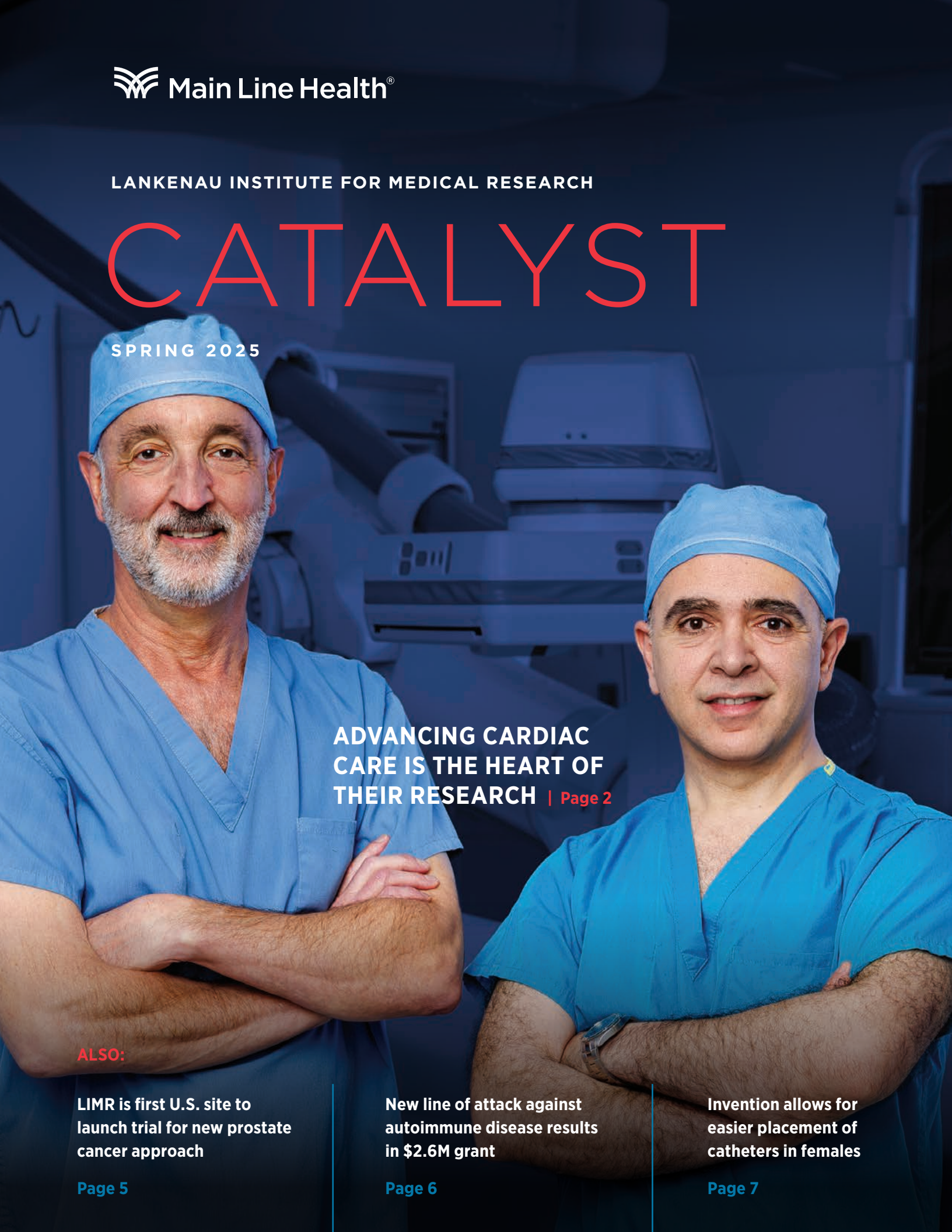

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Lankenau Institute for Medical Research (LIMR) is a nonprofit biomedical research institute located on the campus of Lankenau Medical Center and is part of Main Line Health. Founded in 1927, LIMR's mission is to improve human health and well-being. Using its ACAPRENEURIAL™ model that integrates academic and entrepreneurial approaches, faculty and staff are devoted to advancing innovative new strategies to address formidable medical challenges including cancer, cardiovascular disease, tissue regeneration, gastrointestinal disorders, and diabetes, arthritis and other autoimmune diseases. LIMR's principal investigators conduct basic, preclinical and clinical 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.

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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

Cardiac research is now LIMR's centerpiece

Research into cardiac trials has always been a strength of Lankenau Institute for Medical Research (LIMR) during my 21 years as President and CEO. For that, I am deeply thankful to Peter Kowey, MD, for decades of leadership at LIMR and service as one of the world's leading experts in arrhythmias. With the arrival of William Gray, MD, in 2016 and Basel Ramlawi, MD, in 2019, our program was elevated even further. Cardiac research is now LIMR's centerpiece and, with their major publications and speaking engagements at leading conferences, has a national profile.

We feature Dr. Ramlawi and Dr. Gray in this edition of *Catalyst* to showcase their pivotal role. As co-Directors of the Lankenau Heart Institute, they provide the setting for LIMR's pioneering trials and, as a result, our patients benefit from the types of treatment opportunities not seen in most health systems.

Dr. Gray has served as national principal investigator for many first-in-human trials, allowing developers to assess new medical devices before extensive testing. He is a leader in testing devices aimed at preventing stroke, the fifth-leading cause of death in the United States, with his latest groundbreaking efforts coming in carotid artery disease treatment.

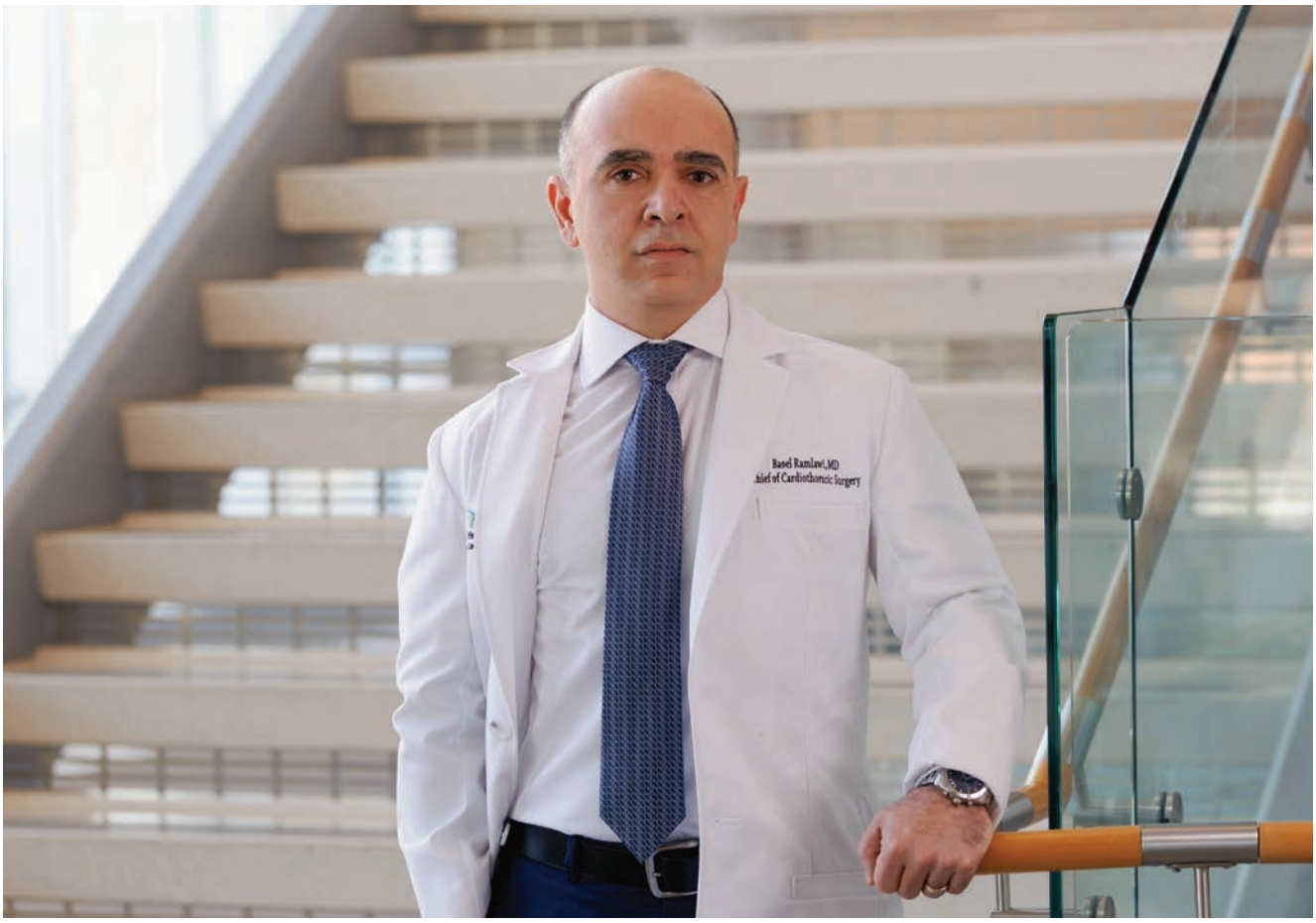
Dr. Ramlawi's work with transcatheter aortic valve replacement (TAVR) has been nothing short of extraordinary. Because of research conducted partly at LIMR, he has helped bring aortic valve treatment to not just the oldest and sickest patients but to lower-risk, younger individuals.

This edition also highlights Laura Mandik-Nayak, PhD. Her investigative work toward finding the answers for rheumatoid arthritis and other autoimmune diseases has resulted in a five-year, $2.6 million federal grant. This research is particularly exciting to me as it builds on my joint research with Alexander Muller, PhD, on the enzyme indoleamine 2, 3-dioxygenase 2 (IDO2), which we originally identified years ago as a target for ways to treat cancer.

Dr. Mandik-Nayak has determined that IDO2 is a probable key actor in autoimmune disease. She is taking a novel approach to seek another target upstream or downstream along the IDO2 pathway. Positive results could lead to treating autoimmune diseases with a drug taken orally.

Lastly, we focus on the exciting invention of Tanara Boursiquot, MSN, RN. In partnership with Lankenau Ventures, LIMR seeks to use the innovativeness of Main Line Health frontline nurses and turn them into inventors. Boursiquot has devised the Accu-Catheter Kit, which enables a nurse or caregiver to reliably insert a catheter in a female patient in a single attempt without assistance. Using the kit can prevent urinary tract infections as well as save time and reduce waste from failed attempts to place the catheter. We look forward to developing and commercializing this invention, making it available to nurses everywhere.

I hope you enjoy reading this edition.



Basel Ramlawi, MD, is a leader in advancing transcatheter aortic valve replacement.

Advancing cardiac care is the heart of their research

DR. WILLIAM GRAY AND DR. BASEL RAMLAWI LEAD THE WAY IN DEVELOPING CUTTING-EDGE CARE UNAVAILABLE IN MOST HEALTH SYSTEMS

William Gray, MD, remembers exactly when his desire to do more than individually treat patients began. He was a Fellow at Brown University in 1989 when the Chief of Cardiology asked whether he had considered research after graduation.

No, I'm not really interested in research," the young physician said.

"Oh, I see," the Chief replied, leaning back in his chair. "You want to only take care of patients one at a time."

"It's funny," Dr. Gray thinks back now. "I don't think that would have resonated so much with many other people, but for me, it crystallized the value of research."

Basel Ramlawi, MD, was 11 when his father developed stomach cancer. He immersed himself in helping his father fight the disease, and by the time he was finishing high school, he was assisting an oncologist with research projects. At McGill University in Montreal, the chance to learn from an expert surgeon made him realize that operating on patients was his calling. Ultimately, he was pulled into the cardiovascular field by the swift, positive impact a surgeon can have. He trained with some of the best in the field, including in Paris under Alain Carpentier, known as the "father of mitral valve repair."

"Being in the operating room is where it all came together," Dr. Ramlawi says. "It allowed me to coalesce the medical field, the sciences, research and the human aspect. You're

taking care of this patient. Their families are waiting outside. It's an enormous, rewarding responsibility."

From those beginnings, Dr. Ramlawi and Dr. Gray are now a resident faculty duo that has spearheaded Lankenau Institute for Medical Research's (LIMR) cardiac research to new heights. As co-Directors of the Lankenau Heart Institute, they provide the setting for LIMR's pioneering trials, creating opportunities in patient care that are unavailable in most health systems. (Lankenau Heart Institute and LIMR are both on Lankenau Medical Center's campus.)

"The leadership, innovativeness and skill of Dr. Gray and Dr. Ramlawi have transformed what was already a strong cardiovascular program into the backbone of LIMR's research efforts," says George Prendergast, PhD, President and CEO of LIMR. "When patients are looking for high-quality care, it resonates when the physicians conduct research that allows them to perform cutting-edge procedures not offered elsewhere. And when your clinical leaders value research, it produces a halo effect that attracts more talent and enhances your program even further."

Leading first-in-human trials, focusing on stroke prevention

In addition to his role at LIMR, Dr. Gray is also the System Chief of the Cardiovascular Division at Main Line Health, a Professor of Medicine at Thomas Jefferson University and holder of the Phillip D. Robinson Endowed Chair in Cardiovascular Medicine. He came to LIMR and Lankenau Heart Institute in 2016 and has been the national principal investigator for numerous trials. Many are first-in-human trials, allowing developers to assess new medical devices before extensive testing.

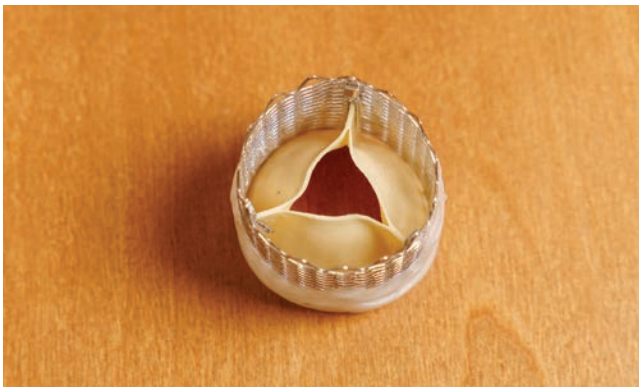
"We were able to contribute to those types of trials just as the technology started to appear," the interventional cardiologist says. "The Food and Drug Administration was interested in safety and effectiveness, and we were well-situated to ride that wave by virtue of our excellent patient care and strong reputation as a research center. It's been a great experience I could not have imagined when starting out 35 years ago."

He initially focused on coronary research, leading to the development of bare metal stents and then drug-coated ones to keep blood flowing. He branched into treating vascular diseases, such as those affecting the legs, kidneys and aorta. Now, he works to develop devices to treat valve disorders and other structural heart conditions.

His longest sustained research effort has drawn considerable attention nationally: advancing the treatment of carotid artery disease to prevent stroke.

Advancing minimally invasive aortic valve replacement, honoring his father's memory

Dr. Ramlawi, Chief of Cardiothoracic Surgery at Main Line Health, has been a leader in advancing transcatheter aortic valve replacement (TAVR). The procedure is minimally invasive, entailing smaller incisions than open-heart valve surgery, and is used to replace narrowed aortic valves that don't open fully. As a national principal investigator, he has worked to broaden TAVR's use nationally and internationally to treat the bicuspid valve and lower-risk patients.



Willliam Gray, MD, holding an artificial valve (seen in detail below) typically used in interventional cardiac procedures.

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William Gray, MD, and the Lankenau Heart Institute team perform procedures as part of numerous first-in-human Lankenau Institute for Medical Research trials.

"The procedure has brought aortic valve treatment to the masses," Dr. Ramlawi says. "Initially, it was brought to the sickest, oldest and most frail individuals. Through research done partly at LIMR, I was able to help bring this to lower-risk, younger individuals."

Dr. Ramlawi was driven to make his father proud, and he succeeded. His father got to see him graduate from medical school before dying from cancer. Now, in addition to a busy surgical practice, he spends his time teaching and developing novel approaches and devices to treat heart valves and aortic aneurysms with the least invasive, most durable approach.

Disseminating their knowledge

The results of Dr. Gray's and Dr. Ramlawi's combined research and clinical prowess extend beyond the Philadelphia region. LIMR cardiac researchers have increased their publication production sixfold since 2019. Dr. Gray frequently speaks at national and international conferences about the advances in clinical trials he has led.

Dr. Ramlawi flew to Osaka and worked with a heart care team on performing Japan's first transcatheter mitral valve replacement.

They have found that their perspective on medicine has changed similarly over the years. To them, decisions are not just about patients' longevity.

"You have to ask what their goals in life are," Dr. Gray says. "Some people want to live long enough to see their kids and grandkids get married or be able to take a hike with those grandkids. A lot of people don't worry so much about longevity, but their quality of life."

Now, they are focused on keeping Lankenau Heart Institute at the forefront of patient care and LIMR at the forefront of research to ensure the latest in technology continues.

"I see an even rosier future," Dr. Ramlawi says. "I'm very happy Bill and I are so aligned on our vision for LIMR and Lankenau Heart Institute. Best-in-class care is our goal. That's what patients should expect from us, right?"

LIMR is first U.S. site to launch trial for new prostate cancer approach

Charles J. Link, MD

Earlier this year, Lankenau Institute for Medical Research (LIMR) became the first site in the country to open the LEGION-100 trial in cancer immunotherapy.

SYNC-T/SV-102 therapy is a new device/drug combination approach to treat advanced drug-resistant cancers through cryoimmune vaccination. The phase 2a clinical trial, sponsored by Syncromune, Inc., focuses first on patients with metastatic prostate cancer but is expected to eventually expand to patients with metastatic breast cancer and other advanced solid tumors. The trial will examine safety and appropriate dosage.

The combination therapy involves inserting a probe into the tumor to freeze a portion of it. The freezing causes the cells to rupture, helping to activate the immune system. A combination of four immunologic agents is then infused into the area, attacking cancer cells throughout the body.

Results of a phase 1a trial were so promising that the American Association for Cancer Research had Charles J. Link, MD, a LIMR Adjunct Professor and co-Founder and Executive Chairman of Syncromune, present them at its 2024 annual meeting. George Prendergast, PhD, President and CEO of LIMR, is a member of Syncromune's Scientific Advisory Board.

MAN ON A MISSION: Lankenau Institute for Medical Research Professor **Scott Dessain, MD, PhD,** was part of a 35-member team to go on a medical mission to Ghana, providing free medical and surgical care. The team, primarily from Lankenau Medical Center, screened 1,131 patients for various medical conditions over four days. Those diagnosed with potential health risks received immediate medical attention.

Hospital-acquired infections, new virus studied by Dr. Sunil Thomas

Sunil Thomas, PhD

Sunil Thomas, PhD, a Lankenau Institute for Medical Research faculty member, published an important study on hospital-acquired infections (HAIs) earlier this year. He also presented on a new virus with the potential to cause a pandemic.

HAIs are often antibiotic-resistant, leading to complications and increased mortality. Dr. Thomas led a study demonstrating the use of a biosimulator to profile microbiomes — communities of microorganisms such as fungi, bacteria and viruses — in intensive care units (ICUs). The study reveals that ICU microorganisms closely resemble patients' microbiomes, with stronger interrelationships under ICU conditions. Combined, the biosimulator and profiling can help understand microbiome changes in settings at high risk for HAIs.

Dr. Thomas also presented a paper on the protein structure of the Camp Hill virus at the Institute for Infectious and Zoonotic Diseases Seminar (University of Pennsylvania) in March.

Camp Hill virus is the first henipavirus reported in North America. It was recently detected in shrews in Alabama. In other regions, henipaviruses have caused serious disease and death in people and animals.

New line of attack against autoimmune disease results in $2.6M grant

Treating cancer with chemotherapy is a balancing act. Chemotherapy drugs kill the patient's cancer cells, but the treatment is toxic to the immune system. In their vulnerable state, patients have to avoid others who may have the flu or other diseases, particularly children, who tend to be a petri dish for infections. The consequences of catching an infection can be serious, even deadly.

Laura Mandik-Nayak, PhD, and her Lankenau Institute for Medical Research (LIMR) team are facing a similar challenge as they seek to treat rheumatoid arthritis (RA). They are searching for a strategy that will prevent the immune system from going into overdrive and attacking the body itself, but they don't want to leave the patient's immune system so weakened it can't fight off other diseases.

It's a challenge the National Institute of Arthritis and Musculoskeletal and Skin Diseases wants her to tackle. It recently awarded Dr. Mandik-Nayak a five-year, $2.6 million grant to explore enzyme indoleamine 2, 3-dioxygenase 2 (IDO2), identified in her preclinical research as a probable key player in autoimmune disease. This time, she is taking a novel approach, seeking another target upstream or downstream along the IDO2 pathway. If she succeeds, she hopes to eventually be able to treat autoimmune conditions with a small molecule that perhaps could be a drug taken orally.

Laura Mandik-Nayak, PhD (left), and Lauren Merlo, PhD, are conducting cutting-edge research into autoimmune disease.

"The holy grail in autoimmune disease research is how to get the immune system to stop attacking itself but still protect you from viruses and any sort of pathogen you might encounter," she says. "That's what we're after."

Laura Mandik-Nayak, PhD

Treating RA is the main goal. It affects around 1% of the world population and can begin at any age, although the chance of onset is highest for those in their 60s. Women are two to three times more likely to develop the condition than men. Although the focus of her grant is on RA, its similarities to other autoimmune diseases have her believing the treatment may extend to those diseases as well.

There is one key difference between chemotherapy and treating autoimmune disease. With chemotherapy, Dr. Mandik-Nayak says, patients are given treatments in cycles, getting time off in between, and only for a limited duration. For autoimmune patients, however, the treatment usually needs to be lifelong.

Autoimmune diseases have proven enigmatic. Once the enzyme IDO2 was identified, the obvious solution seemed to be to attack its enzymatic behavior. As the years passed, she and colleagues Lauren Merlo, PhD, and Weidan Peng, PhD, have progressed toward a different answer — assisted by George Prendergast, PhD, President and CEO of LIMR, Alexander Muller, PhD, and James DuHadaway.

"We think it's a nonenzymatic mechanism that is more important for IDO2's autoimmune function," Dr. Mandik-Nayak says. "We think if we can distinguish between IDO2's pathogenic and protective immune functions by developing a therapeutic that specifically hits the nonenzymatic pathway, we have the potential for a treatment with fewer side effects."

"We have a lot more to do," she adds, "but we feel we're on the right track."

Invention allows for easier placement of catheters in females

As an advanced nurse clinician, Tanara Boursiquot, MSN, RN, frequently heard nurses express frustration about inserting urinary catheters in female patients. With only one hand available to place the catheter while the other positions the patient, they often struggle, at times needing multiple attempts and help from a second nurse or a home health aide.

So Boursiquot had an idea. She conceived of the Accu-Catheter Kit, allowing a nurse to insert a catheter reliably in one attempt without assistance. It is now in prototype, making Boursiquot the latest inventor for Lankenau Institute for Medical Research (LIMR), part of Main Line Health.

"It feels different being referred to as an inventor," says Boursiquot, now a Main Line Health HomeCare Manager. "I'm humble and low-key. I don't seek a lot of attention. But it's exciting at the same time."

The Accu-Catheter Kit is one of several inventions being developed by LIMR through Lankenau Ventures, a joint venture with Early Charm Ventures and L2C Partners.

LIMR seeks to have frontline nurses submit ideas for improving patient care as potential inventions. Boursiquot hesitated for weeks to submit hers but took the plunge. LIMR was glad she did.

The simple U-shaped device retracts the folds of the labia, allowing a nurse to perform sterile insertion with both hands. The Accu-Catheter Kit has the potential to prevent painful and costly urinary tract infections as well as save time and reduce waste from failed attempts to place the catheter. Hospitals, long-term care facilities, home care organizations and women who self-catheterize stand to benefit.

"I really do hope it's effective for nurses," Boursiquot says. "I think it'll be amazing if we can change the way we insert catheters."

Another area where LIMR continues to make invention progress is in mitigating hospital fall injuries. A patent was recently published for a device invented by Barbara Wadsworth, DNP, RN, who is Executive Vice President and Chief Operating Officer of Main Line Health and a longtime nurse. It comprises a sensor capable of detecting when an individual is falling and a compact airbag/cushion-deployment device that can be mounted in various at-risk areas such as a bathroom.

Another fall-safety invention in the patent process is a toilet privacy screen. During his tenure as a Main Line Health executive, Jeshahnton Essex, MBA, MSHA, FACHE — now COO of Baylor University Medical Center — followed Wadsworth's leadership and conceived of a device allowing patients to be supervised to avoid falls yet maintain privacy. The device has an adjustable privacy screen and a lightweight sensor bar that detects any attempt by the patient to get up from the toilet and walk back to bed unsupervised.

The Rogers Limb Support, invented by Colleen Rogers, RN, went on the market in 2024. The device props up a weak or injured limb, enabling a nurse to provide care independently and efficiently without need for assistance from another caregiver. The device is of particular help in caring for patients with diabetes, who frequently have such chronic wounds.

Tanara Boursiquot, MSN, RN, is inventor of the Accu-Catheter Kit (seen in detail below).

Journey of survival and gratitude translates into support for cardiac research

Anne Kennedy felt unwell one February 2022 evening, but not so much that she felt she should cancel dinner plans with friends. "I knew something wasn't right," Anne recalls. "But I could not pinpoint it. Since I was planning to head home right after dinner anyway, I decided to go."

What followed was unimaginable. She collapsed on the sidewalk and her friend called 911. Anne was rushed to Bryn Mawr Hospital, where a CT scan revealed an aortic dissection, a condition in which a tear occurs in the inner layer of the aorta, putting her life at risk.

She would survive, however, launching her on a journey of gratitude that has benefited Lankenau Institute for Medical Research (LIMR) and the work of the doctor who saved her, Basel Ramlawi, MD.

"We wanted to give back to help ensure that others don't go through what we did," Anne says. "We have experienced cardiac disease with close family members. There must be a way to prevent these conditions through research. Dr. Ramlawi gave me a second chance at life, and we are thankful for that. Supporting research is our way of honoring his heroic efforts and helping to improve cardiac care for future patients." Anne and her husband, Paul, have made a major contribution to support cardiac research since her recovery.

Dr. Ramlawi was the surgeon contacted for an immediate consult upon Anne's arrival at Bryn Mawr Hospital. His team jumped into action. They arranged for Anne's swift transport to Lankenau Medical Center, where she underwent an emergency eight-hour surgery.

Anne's recovery was a long and challenging road, requiring two weeks in the intensive care unit. Yet her determination and the support of her family and medical team helped her regain strength.

"The shock and trauma of that night will stay with me forever," Anne says. "But I am so grateful to Dr. Ramlawi and his team for giving me a chance at life again. Without them, I would not be here today."

Through their donation to LIMR's cardiac research, Anne and Paul aim to support continued advancements in cardiac care, ensuring that future patients receive the same level of lifesaving attention and care that Anne did.

Dr. Ramlawi and William Gray, MD, are co-Directors of the Lankenau Heart Institute and LIMR's leading cardiac researchers (see cover story). Through their leadership, Lankenau Heart Institute provides the setting for LIMR's cutting-edge trials, creating opportunities in patient care that are unavailable in most health systems, including for aortic dissection.

"I think Anne is a hero," Dr. Ramlawi says. "She worked hard to get her life back. Now, the generosity of Anne and her husband to support research can translate into many more lives saved down the road."

Anne has returned to being active in her community, but now she shares her experience to raise awareness of the dangers of aortic dissection. "It is important to listen to your body, and if something feels wrong, do not wait — seek help immediately," she says. "My experience has taught me how quickly life can change, and I want others to be aware of life-threatening conditions like this one."

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.

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 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 aftereffects 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.

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.

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 (click on Giving). You may also call Katie Beddis of the Lankenau Medical Center Foundation at 484.476.8067, or email her at beddisk@mlhs.org.

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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, healthcare facilities and researchers provide patients with primary through highly specialized care as well as access to clinical trials.