



Main Line Health®

LANKENAU INSTITUTE FOR MEDICAL RESEARCH

CATALYST

SPRING/SUMMER 2017

IDO: TWO SIDES OF THE SAME COIN

LIMR scientists make stunning research breakthroughs with the enzymes instrumental in immunity. One turns off immune response to cancer, and the other sends the immune system into overdrive. | [Page 3](#)

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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 and autoimmune diseases, such as diabetes and arthritis. 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.



George C. Prendergast, PhD

*The Havens Chair for Biomedical Research
President and CEO*

*Lankenau Institute for Medical Research,
Main Line Health*

WELCOME

90 Years of Revolutionary Cancer Research

In 1927, Charles Lindbergh made his historic trans-Atlantic flight, work began on Mount Rushmore, and Lankenau Hospital Research Institute (LHRI), predecessor to today's Lankenau Institute for Medical Research (LIMR), opened its doors. Unwittingly, it was the first research center in the country to focus on cancer, which Lankenau scientists studied initially as abnormal wound inflammation—a prescient insight.

Ten years prior, in 1917, pioneering cancer researcher Dr. Stanley Reimann joined Lankenau Hospital as chief pathologist on condition that a biomedical research program be created at the hospital. It was, and between 1917 and 1927 Reimann and his colleagues published over 40 research papers.

With funds donated by Rodman Wanamaker, son of famed retailer John Wanamaker, LHRI formally opened in 1927, with Dr. Reimann at the helm. His vision, along with that of Frederick Hammett, a biologist and biochemist, instilled a basic research philosophy with the novel insight to use wound healing as a model to study cell division in cancer. Dr. Reimann studied how inflammatory processes can stimulate cell division, a groundbreaking concept that later was identified as a trait of cancer.

During the next decades, oncology research at LHRI gained national attention. For example, in 1937 the newly created National Cancer Institute identified LHRI as one of the most significant cancer labs in the nation. In 1952, Sidney Weinhouse, then LHRI's head of metabolic chemistry, was awarded the first grant by the National Science Foundation. In 1953, Lankenau installed the country's first cobalt radiation unit for cancer treatment.

A genetic abnormality found in most patients with chronic myelogenous leukemia was discovered and first described in 1960 by Peter Nowell of the University of Pennsylvania School of Medicine and David Hungerford of the Institute for Cancer Research at LHRI (now known as LIMR). Named the Philadelphia chromosome, it was the first genetic defect linked with a human cancer, and its discovery launched the modern era of molecular genetics in cancer research.

In the 1980s, LIMR's James Mullin discovered how tumor-promoting substances break down organ tissue barriers, contributing to a growing understanding of the crucial role of the tumor microenvironment in cancer. In the 1990s, LIMR's Susan Gilmour and Thomas O'Brien uncovered the molecular explanation of solid tumors' addiction to polyamines, a key cellular nutrient.

In recent years, our labs have studied disease-modifier genes such as IDO, which you can read about in this issue. We also pioneered nanotechnology-based gene therapies that can more specifically kill cancer cells. Beyond the realm of drug discovery, clinical trials of new experimental cancer agents remain a staple of our work. In this issue, you'll learn more about one exciting trial, NCI-MATCH, a precision medicine clinical study that seeks to determine if matching certain drugs to specific mutations in a patient's tumor can more effectively treat cancer, regardless of the cancer type.

Over the years, LIMR's research has impacted studies of cardiovascular disease, gastroenterology, and pulmonary, renal and neurological disorders. But cancer remains a key focus for our researchers. For the past 90 years, LIMR's mission has remained unchanged: To advance human health and well-being. With your support, we will continue to revolutionize biomedical research and advance our scientific discoveries in ways that can most rapidly impact patient care.

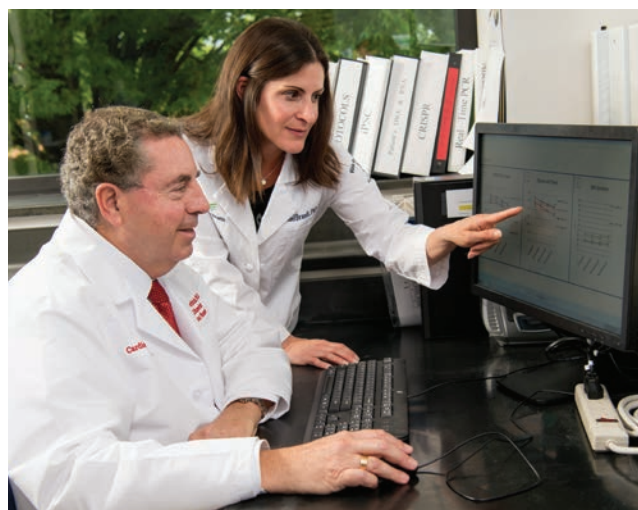
TESTING FOR INHERITED CARDIOVASCULAR DISEASES COULD PLAY A CRUCIAL ROLE IN PATIENT CARE.

A Missing Piece in Heart Care Identified

While patients with a family or personal history of cancer have, for years, been able to undergo genetic testing at Main Line Health to further determine their risk factors, the same has not been true for those worried about their susceptibility for cardiovascular diseases.

But Lankenau scientists and clinicians are working together to see if the time is now right. And while this idea also has been aired elsewhere, only at LIMR are there special scientific capabilities to assess the physiology of what risk a patient's gene variation might confer, especially as it relates to heartbeat abnormalities (arrhythmias).

"With results of genetic testing related to inherited cancer susceptibility, our physicians are able to prescribe certain medications or interventions that can have a real impact on a patient's life. The same concepts could be related to cardiovascular testing," said Rachael Brandt, PhD, manager of Main Line Health's systemwide Cancer Risk Assessment and Genetics Program. "As genetic counseling professionals, we know there are genetic abnormalities related to cardiovascular disease that, if identified, may give us a better idea of how to care for a particular heart patient."



Rachael Brandt, manager of Main Line Health's Cancer Risk Assessment and Genetics Program, and LIMR Professor Charles Antzelevitch discuss the benefits of a genetics program that would help identify patients who may be at risk for developing inherited cardiovascular disease.

106 Genes

Dr. Brandt, a licensed and certified genetic counselor, noted there are approximately 106 genes related to inherited cardiovascular diseases such as cardiomyopathies, arrhythmias and aortic structural changes. "Cardiovascular genetic testing may offer us crucial insights for personalized care, especially for patients who have inherited conditions in which there are no external signs of disease," she said.

LIMR Professor Charles Antzelevitch, PhD, executive director of Cardiovascular Research and director of research, Lankenau Heart Institute, agreed that adding a cardio-genetics program could help heart patients in numerous ways. "Results of genetic testing could point clinicians in the right direction, enabling them to, for example, prescribe appropriate medications, advise patients on lifestyle choices, and monitor them more efficiently," he said. "On the other hand, if genetic testing found that patients did not inherit particular genes, we could alleviate their fears and take a load off of their minds regarding their potential for risk."

In addition to providing for personalized healthcare, "cardio-genetic results could offer an opportunity to identify family members who may be at risk and to intervene and counsel at an early stage of disease, before symptoms appear," said Irving Herling, MD, a cardiologist with Lankenau Heart Institute and Director of Clinical Cardiology for Lankenau Medical Center and Main Line Health.

Dr. Brandt noted that genetic counseling in general has become more widely accepted in American culture in recent years. "Genetic testing is more accessible now, with many labs performing tests at lower costs, improved insurance coverage for counseling and testing, and legislation to help protect patients' rights," she said. "We're at the advent of a new age in healthcare, and many cardiovascular patients could, and I believe should, be included in that."

Additional trends encourage starting such a program, Dr. Brandt continued. "Given Main Line Health's current ranking as a top heart healthcare provider, coupled with the scientific depth present at LIMR, a cardio-genetics program would provide yet another important dimension of multi-disciplinary care for our cardiovascular patients." ✨



LIMR Associate Professors Laura Mandik-Nayak, PhD, (left) a researcher who specializes in autoimmune diseases, and Alexander Muller, PhD, a cancer researcher, are dedicated to unraveling the mechanisms of IDO's actions and translating their findings into effective therapeutic targets.

AS LIMR RESEARCHERS DISCOVERED, THE ENZYMES IDO1 AND IDO2 ARE INSTRUMENTAL IN IMMUNITY. ONE TURNS OFF THE IMMUNE SYSTEM'S RESPONSE TO CANCER CELL GROWTH, AND THE OTHER SENDS THE IMMUNE SYSTEM INTO OVERDRIVE, LEADING TO AUTOIMMUNE DISORDERS.

IDO: Two Sides of the Same Coin

The human body is exquisitely adept at certain functions. You know you're likely to recover from a cold or flu and that a minor cut or scrape will heal. That's a healthy immune system in action.

As a diffuse, complex network of cells, cell products, and cell-forming tissues, your immune system protects your body from pathogens and other foreign substances, destroys infected and malignant cells, and removes cellular debris. Your thymus, spleen, lymph nodes and lymph tissue, white blood cells, antibodies, and lymphokines all play a part in your body's healing process.

Immune cells roam throughout your body, and when rogue agents, such as bacteria, fungi, viruses or cancer cells, are found, your immune fighters target and kill the invaders in a pitched battle worthy of a "Game of Thrones" episode.

But sometimes the invading agent is not recognized at first as dangerous, while other times harmless agents are attacked with unnecessary virulence. And that's when the real trouble begins.

Cancer Detection Gone Awry

Researchers, including those at LIMR, discovered in recent years that the enzyme indoleamine 2,3 dioxygenase (IDO1) drives about half of all human cancers by shielding

the growing tumor from the body's immune attackers. One important job for IDO1 normally is during pregnancy when it helps protect a growing fetus from being attacked by its mother's immune system due to the presence of the father's "foreign" genes in the fetus. IDO1 works with the amino acid tryptophan.

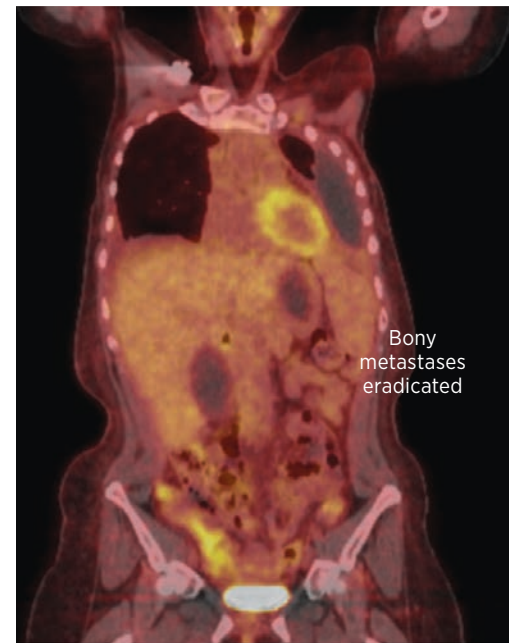
"Scientific evidence shows that IDO1 and the tryptophan biochemical pathway are linked to immune tolerance, meaning they effectively suppress an immune response, and that, unfortunately, can allow cancer cells to grow," said George Prendergast, PhD, president and CEO of LIMR. "Over a decade ago, our work on IDO1 began when we discovered how it becomes widely activated in cancer and how this event leads tumors to escape immune control."

Based on this discovery, Dr. Prendergast and his team began searching more than 10 years ago for drug-like compounds that might suppress the IDO1 enzyme as a strategy to restore immune attacks on cancer cells. Their work led to the discovery of the first IDO1 inhibitors and the demonstration in preclinical studies of their ability to greatly empower the efficacy of many types of cancer therapy. Further, they showed how animals lacking the IDO1 gene were resistant to the development and progression of induced cancers.

Pre-Treatment



One month treatment



After adding an experimental IDO-inhibitor with taxotere, a standard-of-care drug that is often only marginally effective in advanced cancers, a patient with advanced breast cancer that had metastasized to her bones showed a complete regression of her disease there, demonstrating the exciting potential of IDO-inhibitor drugs to improve standard-of-care therapies. PET scan courtesy of Hatem Soliman, MD, of the Moffitt Cancer Center, Tampa, Fla.

Building upon this foundation, several companies are now testing these and other IDO1-inhibitory drugs in cancer clinical trials to determine their effectiveness in treating breast, prostate and other cancers. Early results are promising. "At LIMR we're proud to see growing clinical evidence that our therapeutic approach based on inhibiting the actions of IDO1 can be a viable means to eradicate cancers," said Dr. Prendergast.

Autoimmune Diseases Dissected

While the IDO1 enzyme makes the immune system look the other way to allow tumors to grow, its cousin, IDO2, is much more vigilant. Perhaps too vigilant.

Discovered by LIMR researchers in 2006, IDO2 has been implicated in several autoimmune diseases, such as rheumatoid arthritis, contact hypersensitivity, type 1 diabetes and lupus. IDO2 sends the immune system into overdrive, attacking even healthy cells and causing inflammation.

"We showed that IDO2 acts specifically in B cells, the cell type that produces the autoantibodies required for autoimmune diseases," said Laura Mandik-Nayak, PhD, LIMR associate professor who specializes in autoimmune disorders. "This knowledge is critical for developing new strategies that target IDO2 and thus interfere with the enzyme's ability to drive autoimmune disorders."

Earlier this year, Dr. Mandik-Nayak's team released results of their newest IDO2 study in which they administered an anti-IDO2 monoclonal antibody to mice, and found that those that received the antibody developed only mild rheumatoid arthritis (RA), and in some cases resulted in blocking RA onset all together. The researchers said their results strongly support the theory that IDO2 is a critical mediator of RA development; thus, therapeutic targeting with an IDO2-specific antibody could be used to alleviate disease. For more on this study, see page 6.

Goal: Modulate IDO, Improve Patient Outcomes

The IDOs may be essentially flip sides of the same coin, noted Dr. Prendergast. "One gets the immune system to look the other way, allowing tumors to develop, while the other puts the eye of the tiger into the immune system, helping unleash attacks on healthy tissue and causing inflammatory disorders," he said. "That's why our research to devise viable IDO-modulating therapeutic targets continues in earnest. We know it has real potential to help patients with several debilitating diseases. It's work about which we're passionate, and we're committed to studying its implications for human well-being and longevity." *

INVENTION

DETERMINING INFECTION IN A JOINT REPLACEMENT WAS A MEDICAL CONUNDRUM. ONE ORTHOPAEDIC SURGEON FOUND A BETTER WAY.

Challenge: Accurate Diagnosis of Joint Infection

Conducting basic research is only one of the many imperatives at LIMR. The Institute employs a unique organizational model that integrates the academic world of knowledge and discovery with the entrepreneurial world of invention and translation. Its goal is not just to uncover new scientific principles but to shepherd those discoveries to the patient's bedside.

From 1999 to today, 15 biotechnology companies have been launched from LIMR, and its scientists have been awarded 28 patents for their innovations in healthcare. One of the newest inventions, Synovasure®, is a truly exciting development in orthopaedic care.



Infection vs. Inflammation?

In the United States, approximately 600,000 knees and 400,000 hips are replaced every year, according to the American Academy of Orthopaedic Surgeons. While most of the surgeries provide pain-free function, some patients experience device failure and require more surgery. One reason for the failures is periprosthetic joint infection (PJI), which involves the joint prosthesis and adjacent tissue. Compounding the problem, PJI can be masked by other inflammatory disorders, such as gout and arthritis, making accurate diagnosis difficult.

"Previously if surgeons wanted to test for PJI, they could, for example, send blood and synovial fluid for cell counts, the erythrocyte sedimentation rate and C-reactive protein, and then they'd have to interpret those results; so there was a level of inconsistency among hospitals," said Carl Deirmengian, MD, an orthopaedic surgeon at Main Line Health and a clinical assistant professor at LIMR. "It was a big problem for the orthopaedic field overall."

Dr. Deirmengian figured there had to be a better solution. While other PJI tests searched for either the pathogens themselves or the magnitude of the inflammatory response, he started looking instead at the quality of the patient's actual immune response. His experiments showed that neutrophils, part of the innate immune system, respond in specific ways to infection stimuli. He and his company, CD Diagnostics, found that one peptide released by neutrophils, alpha defensin, was an ideal biomarker for PJI. So they devised a test that could pinpoint alpha defensin in joint-surrounding synovial fluid.

Turns out his test has a sensitivity rate of more than 97 percent and a specificity rate of almost 96 percent, markedly better than other available tests. "Ours was the first research to show in vivo that a specific gene program is induced in neutrophils by infection, but not with other inflammatory disorders," he said. "That helped narrow our search, and led to the discovery that alpha defensin is an ideal biomarker to look for."

Dr. Deirmengian founded CD Diagnostics—incubated at LIMR—to commercialize his findings and the resulting innovation, called Synovasure®. Orthopaedic surgeons can send samples overnight to the lab from their patients whom they suspect have PJI. Within 24 hours their results are ready. Since 2015, the company has tested almost 100,000 samples from hospitals in 49 states and several countries, and is currently conducting a large clinical trial aimed at FDA approval.

For European healthcare providers, Dr. Deirmengian and CD Diagnostics recently took the concept to another level. They developed a lateral flow device, which looks like a home pregnancy test, that surgeons use to test for PJI within minutes, while the patient is undergoing joint replacement. He hopes CD Diagnostics will bring this innovation to U.S. markets soon.

Now a subsidiary of Zimmer Biomet, a global medical device company, CD Diagnostics has moved out of LIMR to Claymont, Del., after that state gave the company a grant to move there. "Synovasure is now being talked about at orthopaedic conferences as a new standard of care. I'm thrilled about that. To be sure, without LIMR, Synovasure would not have been invented," said Dr. Deirmengian. "It was a critical incubator. LIMR gave us the space, lab and support we needed at an important juncture in the product's development." *



"Without LIMR, Synovasure would not have been invented. It was a critical incubator."

—Carl Deirmengian, MD

Updates From LIMR Researchers

Basil Harris, MD, emergency medicine specialist at Lankenau Medical Center and affiliate clinical professor at LIMR, and his team, Final Frontier Medical Devices, took home the top prize of \$2.5 million in Qualcomm's XPRIZE competition. The competition challenge was to invent a Star Trek-inspired tricorder that can diagnose 13 conditions and monitor vital signs. Dr. Harris's self-funded hand-held entry, DxtER (pronounced 'Dexter'), can diagnose 34 conditions and transmit data to medical providers, potentially revolutionizing home health care. His team beat out an amazing number of competitors: 312 other teams from 38 countries. Next steps: clinical trials of the device and other work to gain FDA approval.

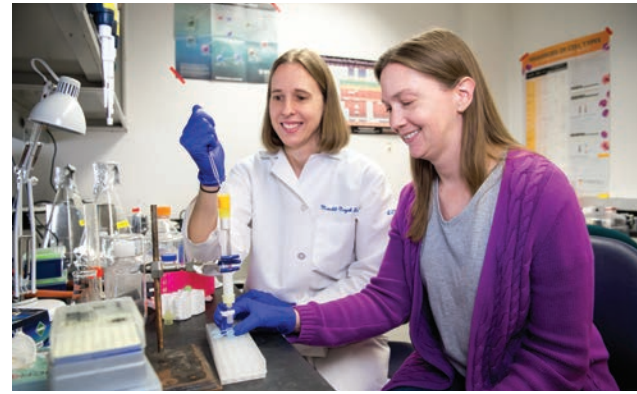
LIMR Professor **Susan Gilmour, PhD**, was awarded two grants to continue her cancer research. A grant of \$611,000 from the U.S. Department of Defense is funding her research on a novel polyamine-targeted therapy to treat melanoma. Another research project investigating the effect of thrombin inhibition to enhance the anti-tumor efficacy of new immunotherapies for ovarian cancer is being funded by the pharmaceutical firm Boehringer Ingelheim.

Sunil Thomas, PhD, LIMR research assistant professor who specializes in immunology, released *Rickettsiales: Biology, Molecular Biology, Epidemiology, and Vaccine Development* (Springer), the first comprehensive book that covers every genera of the order Rickettsiales, small proteobacteria that are known to cause diseases in humans and animals. Insect-transmitted Rickettsiales diseases are significant sources of morbidity and mortality around the world.

Norma Padron, PhD, associate director of the Main Line Health Center for Population Health Research at LIMR, was elected vice chairperson of the Center for Health Organization Transformation (CHOT), an industry-university cooperative research center funded by the National Science Foundation and health organizations. CHOT conducts research supporting major management, clinical, and information technology innovations in healthcare.

The team of **James Mullin, PhD**, LIMR professor who specializes in gastroenterology research, was invited to give two poster presentations at the Digestive Disease Week conference in Chicago in May. One presentation was on the team's studies showing how a protein centrally involved in tissue regeneration could compromise the barrier function of human intestinal epithelial cell layers. The other was on his findings regarding the beneficial effects of orally administered zinc on Barrett's esophagus.

NEWS



(Left) Lauren Merlo, PhD, and Laura Mandik-Nayak, PhD

New Potential Treatment for Rheumatoid Arthritis Discovered by LIMR Scientists

Laura Mandik-Nayak, PhD, LIMR associate professor, and her colleagues developed a new therapeutic approach to treating rheumatoid arthritis (RA). They demonstrated in preclinical studies that a specific monoclonal antibody developed by LIMR associate professor **Lisa Laury-Kleintop, PhD**, both reduced RA's impact and even stopped the onset of the disease.

Current RA medications focus primarily on controlling the inflammation—that is, on treating the symptoms rather than blocking the pathogenic mechanisms that underlie RA development. The researchers theorized that specifically targeting enzymes that modulate the immune response could provide a useful therapeutic strategy to treat autoimmune disease. IDO2, an enzyme discovered by LIMR scientists, promotes inflammation in autoimmune disorders and was an attractive target for antibody therapy development.

"We administered Dr. Laury-Kleintop's anti-IDO2 monoclonal antibody to our aggressive preclinical mouse model of arthritis, and found that those that received the antibody developed only mild disease in their joints," said **Lauren Merlo, PhD**, lead author of the study and research assistant professor in Dr. Mandik-Nayak's lab. "This result builds on our lab's previous work demonstrating that IDO2 was important to the disease process at the genetic level and was especially promising because it extended to multiple preclinical models of arthritis." ✨

Their work to date has been funded in part by the Lupus Research Alliance, the Women's Board of Lankenau Medical Center, and the Zuckerman Family Autoimmune Disorder Research Fund.

CANCER CLINICAL RESEARCH

THE NCI-MATCH TRIAL SEEKS TO DETERMINE IF TREATING CANCERS ACCORDING TO THEIR MOLECULAR ABNORMALITIES CAN BE EFFECTIVE.

National Cancer Treatment Study Available at All Main Line Health Acute-Care Hospitals



Paul Gilman, MD, System Division Chief of Hematology/Oncology at Main Line Health and Interim Director of the Clinical Research Center at LIMR

Being told you have cancer is one of the most frightening moments in life. If you or a loved one has been diagnosed recently, you may be wondering about the next steps. Main Line Health is enrolling patients in a groundbreaking national research trial that places precision medicine at the center of cancer treatment.

National Cancer Institute-Molecular Analysis for Therapy Choice (NCI-MATCH) is a clinical study that seeks to determine if matching certain drugs in adults whose tumors have specific gene abnormalities will effectively treat their cancer, regardless of their cancer type. The trial has been designed for patients 18 years and older who have solid tumors or lymphomas that have progressed, even after standard oral or intravenous therapy, and rare cancers for which there is currently no standard treatment.

To be eligible for the screening portion of the trial, a sample of the patient's tumor is analyzed to determine if it contains genetic abnormalities for which a targeted drug exists. If there's a match, the patient is enrolled, and a treatment is assigned based on his or her specific genetic abnormality (a process known as precision medicine). Trial investigators seek to determine the efficacy of treating cancers according to their molecular abnormalities, rather than the origin of their tumor (e.g., breast, ovary, brain) or tumor type.

NCI hopes to screen 6,000 patients nationwide in the study. As of late April, more than 5,000 had already been screened, including about 70 patients through Main Line Health.

We caught up with Paul Gilman, MD, System Division Chief of Hematology/Oncology at Main Line Health and Interim Director of the Clinical Research Center at LIMR, to ask him about MATCH and how it may help cancer patients and their healthcare providers seeking better treatments.

To learn more about the NCI-MATCH clinical trial at Main Line Health, call 484-476-2649, email CancerTrials@mlhs.org, or visit www.limr.org/NCI_MATCH

Q: What makes the MATCH trial so revolutionary in its scope?

Dr. Gilman: Two things make this unique. First, it's an unusually large trial with a significant number of enrollees and a significant number of investigational drugs being studied. Second, it's being driven by tumor gene mutations as the determining factor for treatment, independent of specific tumor type. That is, it looks at cancer treatments based on genomics, not just on the tumor type and site of origin as has been done in cancer treatment to date. It's looking instead at the genetic level. So, for example, enrollees with breast, lung or liver cancer might all receive the same targeted drug if their tumors have the same genetic mutations present.

Q: You've specialized in oncology and hematology for the past 32 years. What is it about the MATCH trial that you find intriguing?

Dr. Gilman: Notably, it's the access provided to the study's enrollees to tumor gene analysis and even more importantly, to promising medications. This trial could further accelerate drug development in oncology. By looking at tumor genes and, in turn, proteins and the outcome of therapy with drugs that target those, we're really now treating the underlying biology of cancer.

Another exciting aspect is the availability that didn't previously exist of a significant number of targeted drugs to test. This trial couldn't be done until recently, because there simply weren't that many gene-targeted drugs available. However, now a relatively rapidly increasing number of new drugs are being developed.

Q: What do researchers hope to discover from the MATCH trial's results?

Dr. Gilman: Determining the response to therapy based on specific gene abnormalities will help us expand the usefulness of available drugs across tumor types and benefit a larger population of patients. The MATCH trial is part of a significant movement toward more directed therapy. Chemotherapy, long a standard of care for cancer patients, is a broad approach to treatment, one without individualization except in relation to toxicity and side effects. This new approach to treatment, as in the MATCH trial, is a more specific attack based on unique tumor characteristics. This will hopefully result in greater success with the use of "precision medicine." ✨

Through the Generations: Vital Support for Lankenau's Mission

For Peter and Louise Havens, their connection and lifelong love of Lankenau may be traced back further than each of their own lives.

Longtime residents and philanthropic supporters of the community, Louise, her mother, Mary L. Smith, and her late step-father, Bill Smith, received their care at Lankenau. In addition to receiving care here, Mary is a significant benefactor to Lankenau and is a former Trustee of the Lankenau Foundation board. Louise, a graduate of Villanova University, is the Medical Grant Administrator of the W.W. Smith Charitable Trust. In her role, Louise has overseen and directed tens of millions of dollars to support medical research, including significant investments at Lankenau Medical Center and LIMR.

Most notable of these gifts was a donation of \$625,000 in 2013 to create a fund to be a bridge of support in the advancement of many pioneering new therapies and tests at various stages of development within LIMR. This fund has allowed LIMR to continue to push ahead and make advancements, even during times of economic and philanthropic uncertainty, where other organizations have had to pull back on such initiatives. In addition to her role at the trust, Louise is also the trustee of the Louise A. Havens Foundation for Diabetes Research and Treatment, which has also provided significant support to LIMR.

Peter's connection goes back several generations, as his great-grandfather, Hermann Hessenbruch, was President of Lankenau from 1901 to 1913 following the passing of John D. Lankenau as President. Peter's grandmother, Florence Dreer Hessenbruch, was the first president of the Women's Board, as well as the founder of the Deaver Auxiliary and the Gift Shop at Lankenau. Peter's father, W. Paul Havens, MD, trained at Lankenau and, with an interest in viral hepatitis and cirrhosis, went on to become a prominent medical professor at Thomas Jefferson University.

Peter, with an undergraduate degree from Harvard and an MBA from Columbia, founded Baldwin Management in 1999 after serving as a member of the Board of Directors and Executive Vice President of the Bryn Mawr Trust Co. His leadership roles within Lankenau and Main Line Health are many: He serves as a Lankenau Medical Center Foundation Trustee, Vice Chairman of the Main Line Health Board of Governors, and Chairman of LIMR's Board of Trustees.



In photo, from left: Robert Havens; Benefactor Peter Havens; Dr. George Prendergast, The Havens Chair for Biomedical Research, and President, CEO and Professor of LIMR; Benefactor Louise Havens.

Most recently, Louise and Peter funded an endowed chair with a \$1 million commitment to create the Havens Chair for Biomedical Research, held by LIMR President and CEO George Prendergast, PhD. In addition to the Havens Chair, they also created the Mary L. Smith Endowed Chair in Pulmonary and Critical Care with an additional \$1 million gift. This chair, held by Donald D. Peterson, MD, was created by the Havens family, including Peter, Louise, Robert, Vicki and Serter in honor of Mary L. Smith. Both of these endowed chair gifts utilized the Lankenau Medical Center Foundation's matching program for approved gifts of \$1 million or more to meet the \$2 million endowed chair threshold.

When family ties to Lankenau are as strong as they are for Peter and Louise, it is hard to overstate their crucial role in making Lankenau Medical Center and LIMR world-class destinations for clinical care, research and education. In many ways it could be argued that their leadership and engagement have been as impactful to Lankenau as the contributions made by their distinguished forebears. ✨

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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.

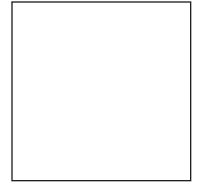
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Main Line Health® is an integrated health system serving the Philadelphia region, with more than 2,000 physicians, one quaternary and three tertiary care hospitals, a wide network of patient care locations and community health centers, specialized 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.