Main Line Health®

LANKENAU INSTITUTE FOR MEDICAL RESEARCH

CATALYST

SUMMER 2022

CLOSER THAN EVER TO REGENERATING NEW TISSUE

The key may soon be unlocked | Page 2

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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.

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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

Cutting-edge innovations in regenerative healing and diabetes care steadily progress

At Lankenau Institute for Medical Research (LIMR), we often talk about how we punch above our weight, achieving successes that are as cutting edge as those of larger biomedical research institutions.

Our cover story is a prime example. Decades of research by Ellen Heber-Katz, PhD, are progressing toward off-the-shelf products that could transform how we think about healing. Pilot studies of one of these products have indicated the possibility of not only restoring wounds but tissues damaged by natural aging.

That kind of innovation has inspired the research community—and donors.

Thanks to a gift of $1 million from The Green Family Foundation, paired with a $1 million match from the Lankenau Medical Center Foundation, The Daniel B. and Florence E. Green Endowed Chair in Regenerative Medicine Research has been established, with Heber-Katz its first holder. The gift ensures her work will continue and grow.

Other examples are in the Focus on Diabetes section, exploring our work with diabetes complications and wound care.

Research into life-threatening diabetes complications such as kidney disease, heart disease and stroke has yet to uncover an effective preventive or treatment. LIMR, however, has pursued a new strategy to target a glucose-derived molecule called 3-deoxyglucosone (3DG) that may be the bad actor causing these complications. Our research into 3DG and its source may alter the landscape on preventing and treating diabetes complications, much as controlling cholesterol did for heart disease.

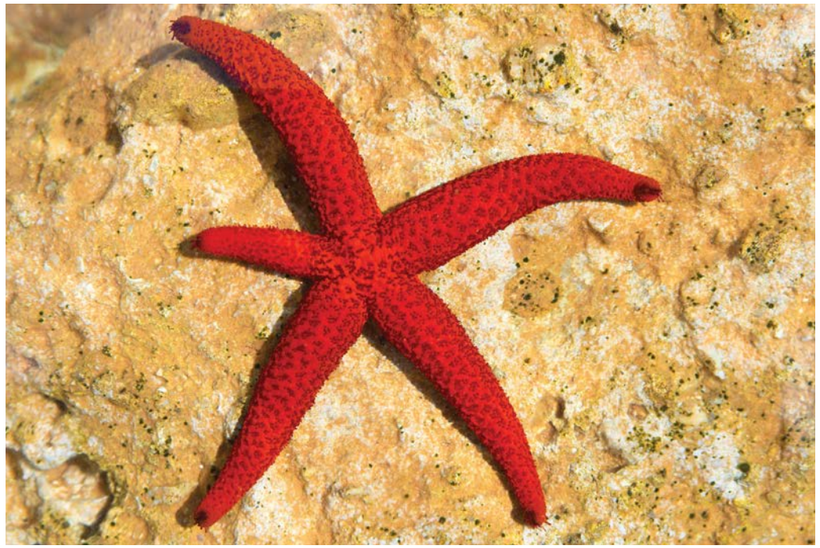
This section also exhibits the fruits of our acapreneurial™ approach, a hybrid program of academic/entrepreneurial biomedical research and development, with a story about Main Line Health nurse Colleen Rogers and her invention of a device to cradle the limb of a diabetic patient during wound care instead of having to find another nurse to hold it up.

Rogers' innovative thinking has led to a simple-to-operate, adjustable device that has been licensed and is being prototyped.

These kinds of smart inventions by frontline health care workers are why Lankenau Ventures, a joint venture formed to accelerate the development and commercialization of inventions conceived by those in the medical field, was formed. Moving original ideas that target improving the patient experience from bench to bedside is at the core of acapreneurialism.

One final development I want to highlight is a technology that will bring new-found capabilities to match cancer patients to clinical trials for new drugs by using the results of doctor-ordered molecular testing. Patient-care options will improve significantly as a result of our agreement with a company called Syapse to bring this platform to Main Line Health.

I hope you enjoy reading about these developments and more.



Starfish are known for their ability to regenerate limbs and even entire bodies.

Closer than ever to regenerating new tissue

MAMMALS LOST THE ABILITY DURING EVOLUTION TO REGROW TISSUE AND STAVE OFF AGING. THE KEY TO RESTORING IT MAY BE UNLOCKED.

In 1996, Ellen Heber-Katz, PhD, accidentally found that a strain of mice could regenerate tissue that is essentially brand new—including nerves, hair follicles and tendons—rather than the product of typical wound repair. It is an astounding trait thought to have been lost by mammals in evolution. The news took off.

By 2002, *New York Times* bestselling author James Rollins made this discovery a central scientific premise of his novel *Amazonia*. He highlighted Heber-Katz and her team, calling their work "an odd and unexpected phenomenon." Four years later, the discovery was in the newspapers, generating headlines such as "Just like Terminator, mouse ears will be back" (*Chicago Tribune*) and "Super-mouse offers clues" (*Winnipeg Free Press*).

Heber-Katz joined Lankenau Institute for Medical Research (LIMR) in 2014 to lead the Laboratory of Regenerative Medicine and accelerate progress toward useful application of this research. The science is no less exciting as they move closer to clinical trials in chronic wound healing and regenerating bone lost to periodontal disease.

Ellen Heber-Katz, PhD

Heber-Katz's success led to her being named last year as inaugural chairholder of The Daniel B. and Florence E. Green Endowed Chair in Regenerative Medicine Research at LIMR. The chair was made possible with a gift of $1 million from The Green Family Foundation, paired with a $1 million match from the Lankenau Medical Center Foundation through its matching initiative designed to encourage large-scale, transformational philanthropic commitments.

"The funding has come at a critical stage, just as we are moving from the lab into the clinic," Heber-Katz says. "I deeply appreciate the Green family's generosity and pledge to keep advancing this cutting-edge research."

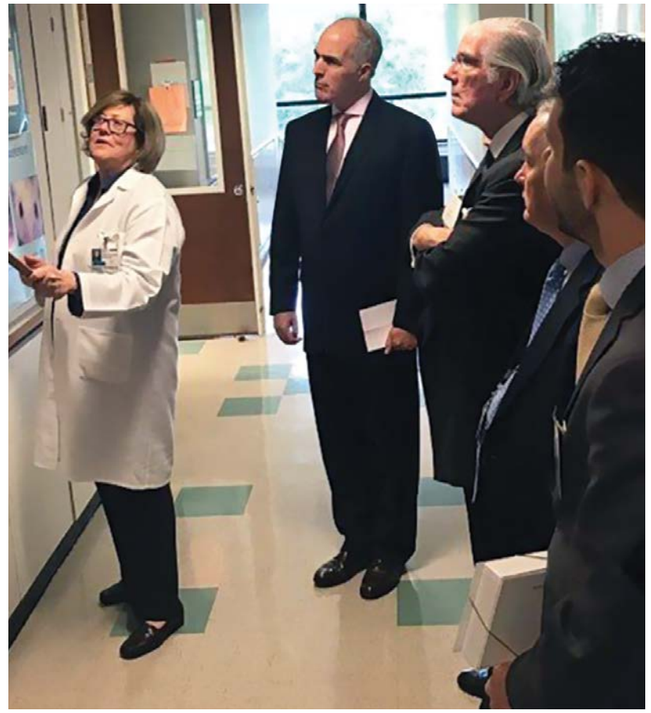
A shocking discovery

Her research began at the Wistar Institute when she accidentally discovered that a larger-than-usual strain of mice called MRL (Murphy Roths Large) could completely heal small holes in their ears without scarring (ear holes normally last a lifetime and help to distinguish mice during research studies). The holes healed in only a few weeks.

"I couldn't believe it when I first saw that the ear holes were completely gone," she says. "In repeating the experiment, the tissue regenerated like new again."

The scientific world took notice of her work in 1998 at the annual meeting of the American Association for the Advancement of Science. *Science*, the association's journal, had just devoted an issue to describing how regeneration was seen only in starfish and amphibians such as salamanders, with rare exceptions in mammals (for example, antler regrowth in deer).

"The organizers thought my presentation on regeneration would echo that line of thought—how mammals can't regenerate, but amphibians can," recalls Heber-Katz. "People were stunned."



Ellen Heber-Katz, PhD, explains how her research on regenerative tissue growth in mice is leading to hope for regeneration in humans for U.S. Senator Robert Casey, LIMR Board Chair Peter Havens and other guests in 2017.

In 2006, the "Terminator" headlines took off as Heber-Katz and colleagues discovered that mice lacking the p21 gene gain the ability to regenerate tissue. But this gene was part of a bigger picture. Her team later found that the pathway leading to regeneration was controlled by a single master molecule known as hypoxia-inducible factor 1 alpha (HIF-1a), a central controlling gene that unlocks regeneration in mice. Using a drug to upregulate HIF-1a during wound healing, Heber-Katz's research team showed that normal nonregenerating mice could regenerate just like the original MRL mice.

Hope for nonscarring regenerative healing

The current phase of Heber-Katz's work builds upon these findings, focusing on disease models that could be addressed by drugs that increase HIF-1a.

Major federal grants followed as Heber-Katz's lab branched out into other areas of medicine. The Department of Defense's interest was piqued by the possibility of limb regeneration in the context of wartime injuries. Through a grant from the department and collaboration with the Curtis National Hand Institute and Johns Hopkins University, progress is being made on digit regrowth and restoration of nerve function in mice and rats. Also, with support from the National Institute of Dental and Craniofacial Research (NIDCR) and the National Institute on Aging, she has worked on the effects of the regeneration drug on osteoporosis and healing chronic wounds in aged animals.

"Chronic nonhealing wounds are a severe problem for older people and those with diabetes, often leading to amputation," Heber-Katz says. "It came as a big surprise that upon applying our drug topically in mice, there was dramatic healing without scarring and their hair grew back."

The NIDCR provided funding as she moved into periodontal disease, which affects a majority of Americans at some point in their lifetime. In collaboration with the University of Pennsylvania School of Dental Medicine, she found that her lead compound totally regenerated lost bone in a mouse dental model of the disease.

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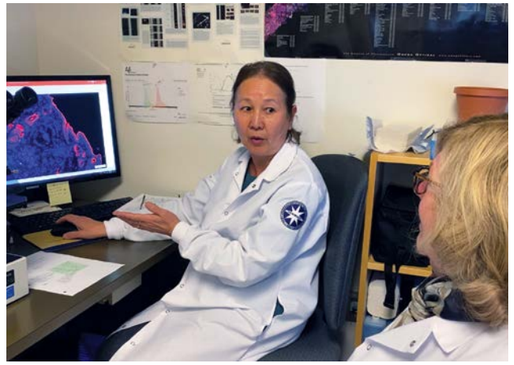
Drugs to address diseases and aging

Heber-Katz is developing several new drug formulations that offer hope for nonscarring regenerative healing. One is a systemically deliverable hydrogel for treating internal wounds that could prove an off-the-shelf option as opposed to stem-cell approaches being researched. Pilot studies suggest the hydrogel, which would be injected under the skin, may restore not just wounds but tissues damaged by natural aging processes. Heber-Katz and her research colleague at the University of California-Berkeley received a patent for the product in 2021.

Another product is a suture infused with a compound that would limit scarring of a surgical wound. It, too, would be an off-the-shelf option. The patent is expected to be issued shortly.

Says George Prendergast, PhD, president and CEO of LIMR, "Unlike most strategies for tissue regeneration, which are based on implanting or transplanting stem cells, Ellen's approach offers an off-the-shelf option that represents true FDA-approvable medicine. Perhaps even more intriguingly, she has found that the application of her approach in aged animals seems to produce a rejuvenating effect, stimulating an anti-aging phenomenon. How durable this effect may be is not yet clear, but we'll soon be ready to do the studies."

What's next for Heber-Katz and her collaborators at the University of California-Berkeley, Penn and Hopkins? She has little doubt it will be treatments for humans.



Kamila Bedelbaeva, PhD, shows an image of mouse tissue that she has stained for stem cell markers to Ellen Heber-Katz, PhD.

"In the relatively near term," she says, "I believe there will be regenerative drugs for humans."

...

Heber-Katz has received federal funding for 80% of her research, totaling $10.2 million. The remaining 20% and $2.2 million is financed by nongovernmental resources. ✷

Images of a mouse heart from an ordinary nonregenerating mouse (left) and an MRL regenerating mouse (right) one year after cryoinjury. The ordinary mouse has scarring. The MRL mouse exhibits scarless regrowth.

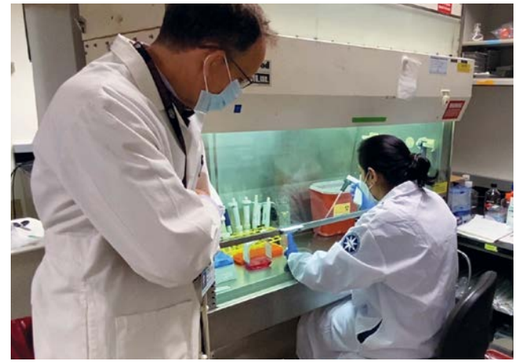
Trip to India focuses on early-warning signs of potential pandemic

For Scott Dessain, MD, PhD, traveling to northeastern India during a pandemic made perfect sense.

The professor with Lankenau Institute for Medical Research is recognized for his expertise in using monoclonal antibodies to detect and treat infectious diseases. And the city of Shillong is in the type of zone where scientists have determined pandemics are most likely to originate. Regions where people increasingly interact with wildlife amid rapidly shifting environments increase the risk of animal-to-human infection.

Dessain was invited by Shillong's public health institute to speak on the detection of infectious diseases. Ultimately, the goal is for them to conduct such work independently—and be able to alert global health officials if they uncover a new pandemic threat.

Epidemiologists have mapped out parts of the world that are vulnerable to animal-to-human infections. These maps led Dessain to consider visiting India. ✷



Scott Dessain, MD, PhD, in the lab with Fetweh Al-Saleem, DVM.

WATCH THE VIDEO: To learn more about this story, scan the QR code.

High-powered technology to use genetic test results to match cancer patients with clinical trials

An innovative technology is coming to Main Line Health that will take the results of molecular testing and quickly match cancer patients to relevant clinical trials.

Lankenau Institute for Medical Research (LIMR) and Main Line Health are working with San Francisco-based Syapse to bring the Syapse Learning Health Network and multisource data platform to the health system. Based on genetic mutations identified in testing ordered by their oncologists, patients will be matched by the Syapse platform to any clinical trials underway at Main Line Health that may be beneficial and also identify suitable trials at other sites across the country.

The Syapse platform will be continually refreshed, incorporating new patient test results and the protocols for any new clinical trials nationwide. LIMR clinical research coordinators will notify the oncologist any time the system flags a patient as eligible for a trial. Patient confidentiality will be maintained at all times.

The platform will also allow Main Line Health to tailor its trials to the community's needs, identifying particular mutations in the local population where opening a trial may be beneficial. ✷

Sunil Thomas, PhD, research associate professor, has released a three-volume set called *Vaccine Design: Methods and Protocols*, Second Edition (Springer Nature) that provides a foundation and new pathways for today's vaccine researchers.

Main Line Health nurse turns inventor to help with wound care

During her three decades as a nurse, Main Line Health's Colleen Rogers has cared for diabetic patients too weak to lift their leg to allow her to change the dressing on foot or limb wounds by herself. She wondered why there wasn't a device to cradle the limb instead of having to find another nurse to hold it up.

Colleen Rogers, RN

For years she had a concept in mind for such a simple-to-operate, adjustable device. However, she never thought of herself as a potential inventor until 2019, when Lankenau Institute for Medical Research (LIMR) put out a call for ideas from frontline health care workers that could be advanced to prototyping and production to benefit patients. The effort to aid diabetes patients and caregivers was on.

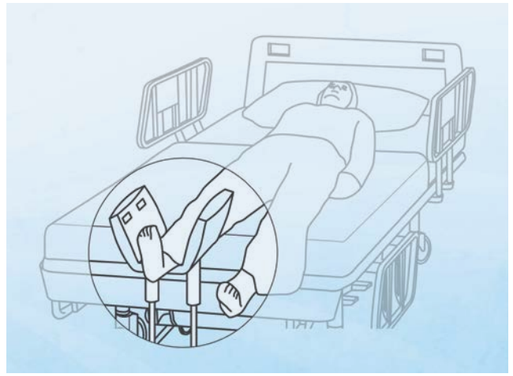
"I was overjoyed to have somebody interested in it," says Rogers, who cares for many diabetes patients at Bryn Mawr Rehab Hospital. "We do so much wound care. For a person with diabetes or other conditions, it's hard to hold your leg up to let us dress the wound if you're not fit, let alone if you're sick and in a hospital bed, or even on a ventilator."

A path to production

Lankenau Ventures, a joint venture formed to accelerate the development and commercialization of inventions conceived by those in the medical field, has licensed the invention and it is moving toward being prototyped. The joint venture includes LIMR; L2C Partners of Wynnewood, LIMR's intellectual property manager; and Early Charm Ventures of Baltimore, a science-oriented invention studio that brings such new devices to market.

More than 37 million Americans, or 1 in 10, have diabetes. Approximately 15% of them develop an open sore or wound called a diabetic foot ulcer, commonly located on the bottom of the foot, which is caused by nerve damage and poor blood flow that can accompany the disease.

Diabetes is the leading cause of lower extremity amputations not caused by trauma. An estimated 14-24% of patients with diabetes who develop a foot ulcer have an amputation,



according to the U.S. Centers for Disease Control and Prevention. Research has shown proper wound care can prevent foot ulcers.

Various limb support devices are on the market to assist with wound care, but some are bulky and difficult to maneuver, and others are intricate and expensive. Some have to be affixed to the hospital bed.

The Rogers Limb Support Device is height- and position-adjustable, allowing any limb to be comfortably supported. Its mobile base can slide underneath a bed, easing use in tight spaces common in a patient room. It is also lightweight and mobile. A patent application has been filed for the device.

Caregivers as inventors

"This is exactly the kind of practical, smart concept we were looking for when we asked nurses to provide their ideas for new inventions," says George Prendergast, PhD, president and CEO of LIMR. "Patients and caregivers stand to benefit, and I believe hospitals and other medical facilities will be eager to put it to use."

Another reason Rogers' device caught LIMR's attention was the potential to help health care facilities save on personnel and cost, reducing the occasions when two caregivers would be required to attend to a patient instead of one.

"This was an idea in the back of my head, and now I have people working on this to help nurses and patients," Rogers says.

WATCH THE VIDEO: To learn more about this story, scan the QR code.

With $1.67M federal grant, LIMR pursues new approach to preventing life-threatening diabetes complications

One hundred years ago, a 14-year-old boy named Leonard Thompson was near death from diabetes, only to be saved when he became the first human to receive insulin to reduce blood sugar. Since then, numerous advances have been made in managing diabetes through lowering glucose.

Despite those advances, little has been accomplished against potentially life-threatening diabetes complications, which place patients at increased risk of kidney disease, heart disease, stroke and other serious conditions.

Lankenau Institute for Medical Research (LIMR) scientists, however, believe they have identified a molecule that holds a key to preventing life-threatening diabetes complications. The research team is studying the effects of a glucose-derived molecule called 3-deoxyglucosone (3DG) that has seen relatively little investigation to date.

Lower glucose levels not enough

"While scientists have focused on developing drugs to lower glucose levels in the bloodstream, they have not targeted 3DG as a bad actor," says George Prendergast, PhD, president and CEO of LIMR and co-principal investigator for the program. "Indeed, recent research has shown that intensive glucose control does little to reduce complications for most diabetic patients. Innovative drugs that safely lower 3DG may hold the key to preventing diabetes complications such as heart attacks, kidney failure, liver disease and wound healing that proceeds slowly or not at all."

Their research is being funded by a three-year, $1.67 million grant from the National Institute of Diabetes and Digestive and Kidney Diseases.

LIMR scientists will investigate a source of 3DG production that might explain its elevation in diabetic patients and seek to identify new drug candidates that can block production of the disease-causing molecule. Ideally, this research will lead to predictability and prevention of diabetes complications much like the discovery of cholesterol did for heart attacks.

"The grant supports establishing how 3DG is produced within cells and the effect of this production on diabetic complications," says Melvin Reichman, PhD, senior investigator at LIMR and co-principal investigator. "It also supports learning how certain food components may increase 3DG production and identifying new drug candidates that lower levels of 3DG as an innovative therapeutic strategy."

Melvin Reichman, PhD

Lisa Laury-Kleintop, PhD

3DG levels tied to complications

More than 37 million Americans overall—just over 1 in 10—have diabetes. An estimated one-third of them have chronic kidney disease, according to the U.S. Centers for Disease Control and Prevention.

Several clinical studies confirm that these patients have significantly higher 3DG levels than healthy individuals and that patients with more severe complications have the highest 3DG levels. LIMR scientists have collected initial evidence that 3DG levels in those cells far exceed those in blood serum. They seek to confirm their hypothesis that 3DG is a cause of kidney disease in diabetics and can serve as a diagnostic biomarker.

Lisa Laury-Kleintop, PhD, LIMR associate professor and expert in preclinical models of diabetes and heart disease, is another key investigator for the project. The LIMR team will be joined by renowned scientists at three other academic institutions for this multidisciplinary project. The research program is 100% federally funded.

Ellen Heber-Katz, PhD, working with colleague Azamat Aslanukov, PhD, in the Laboratory of Regenerative Medicine.

Heber-Katz research inspires the creation of new endowed chair

Ellen Heber-Katz, PhD, has been conducting revolutionary research into anti-aging and tissue regeneration for more than two decades. Lankenau Institute for Medical Research (LIMR) had the good fortune to bring Heber-Katz aboard in 2014, appointing her as the head of its new Laboratory of Regenerative Medicine and providing the resources to help advance her research.

Last year, that work inspired The Green Family Foundation to establish The Daniel B. and Florence E. Green Endowed Chair in Regenerative Medicine Research, with Heber-Katz given the honor of inaugural chairholder in hopes of bringing anti-aging agents and nonscarring healing into society.

Heber-Katz first shocked the scientific world in the 1990s when her research showed that a strain of laboratory mice can regenerate damaged tissue. Soon, she will be able to test a new regeneration drug for its effectiveness in healing chronic wounds and treating diseases of aging in humans.

Most strategies for tissue regeneration are based on implanting or transplanting stem cells. However, her approach offers an off-the-shelf option that represents FDA-approvable medicine. Further, she has found that her approach in aged animals seems to produce a rejuvenating effect, stimulating an anti-aging phenomenon. Upcoming studies will examine the durability of this effect.

The Daniel B. and Florence E. Green Endowed Chair in Regenerative Medicine Research was established with a $1 million gift from The Green Family Foundation, paired with a $1 million match from the Lankenau Medical Center Foundation.

The late Daniel B. Green was a former trustee of the Lankenau Foundation, beginning his board service in 1976 and named an emeritus trustee in 2009. During his decades-long involvement on the board, he partnered on many initiatives including leading the Tribute Committee of Lankenau's Heart Pavilion Gala and actively supporting many other events to benefit the Lankenau Heart Institute and LIMR. Green was the chairman of Firstrust Bank from 1979 to 2015 and chairman emeritus until his passing in 2020. He was also Firstrust Bank's CEO from 1970 to 1995, when his son Richard Green succeeded him to become President and CEO. Arlin Green, the youngest son of Daniel and Florence Green, currently serves as a Lankenau Foundation board member and as a member of The Green Family Foundation.

The Green Family Foundation is honored to establish this endowed chair and both recognize and amplify the remarkable research efforts of Dr. Heber-Katz.

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.

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 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.

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.

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 Amy Mansky of the Lankenau Medical Center Foundation at 484.476.8070, or email her at manskya@mlhs.org.

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Main Line Health®

ABOUT MAIN LINE HEALTH

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