Next Generation: Young Investigators Search for Cures
Dear Friends,

It is my pleasure to present you with the latest issue of *Lerner Research Institute Magazine*. In this issue, we turn our attention to our young investigators, whose talents and innovative ideas are leading to exciting breakthroughs and are paving the way for the cures of tomorrow.

Young investigators are essential to the success of scientific research. They bring fresh perspectives and creativity into the labs, finding new ways to think about and solve old problems. But with the declining federal research budget (see infographic below), young researchers often lack the funds to cultivate their most creative ideas. They are often forced to focus on proven experiments that have a higher likelihood of receiving federal support, leaving their innovative projects unexplored. Unfortunately, this has become the “new normal” in research.

At the Lerner Research Institute, however, we recognize that without innovative science, there would be no cures. That’s why we established the Lerner Research Institute Chair’s Innovative Research Fund to support creative research projects that have great potential for improving public health. The program provides philanthropic funding to help our researchers gather enough preliminary data to submit a competitive federal grant proposal. For example, Christine McDonald, PhD, who you will read about on page 12, received the Chair’s Innovative Research Fund support in 2011 and went on to secure a major grant from the U.S. Department of Defense to continue her groundbreaking studies in the genetics of Crohn’s disease.

The investigators profiled in this issue study very different diseases, but they share a common goal: to advance scientific discovery and improve the lives of our children and grandchildren. Our investment in their work is an investment in our future.

With warmest regards,

Paul E. DiCorleto, PhD
Sherwin-Page Chair
Lerner Research Institute

“Young investigators are essential to the success of scientific research.”

— Paul E. DiCorleto, PhD

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**Budget Cuts Threaten Biomedical Research**

- **PROBLEMS CAUSED BY LACK OF FUNDING**
  1. Lifesaving programs left without support
  2. Biomedical community risks losing talented scientists
  3. Students deterred from choosing careers in research

As funding for research grants disappears, philanthropy is more important than ever to generate life-saving discoveries.

[www.clevelandclinic.org/giving](http://www.clevelandclinic.org/giving)
Embodiment is the sense that our limbs belong to us. Touch, vision and the brain work together to create this sense, and when touch is lost or altered, changes to limb embodiment can occur. This image shows a temperature map of a hand before and five minutes after a perceptual illusion that alters touch and embodiment. The sense that our limbs belong to us is called embodiment. When the brain no longer feels the “right” touch, the limb becomes disembodied, blood flow slows and the limb rapidly cools down. **Paul Marasco, PhD,** of the Department of Biomedical Engineering, uses these cognitive neuro-engineering approaches to build prosthetic limbs that feel like they are part of the body.

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Philanthropy is Crucial for the Future of Medicine

America’s tradition of philanthropy has enriched our lives in countless ways. Consider its critical role in the success of American medicine, where it has led to longer lives, better quality of life and lower mortality from major diseases.

Now, as healthcare costs escalate, reimbursements shrink and federal funding for research declines, philanthropy is more crucial than ever. It will make the difference between good care and great care.

Giving has almost as many motivations and expressions as there are donors. Some hope to alleviate suffering, some to promote progress and yet others to bring about a more just world. Gifts to hospitals and medical centers can achieve all three of these objectives. They support care for the sick and injured; they allow the discovery of new treatments and cures; they promote access to better healthcare for all who need it.

As a surgeon and CEO, I’ve seen the powerful effect of giving on both donors and recipients. Sick children, adults and the families who love them flourish under the favor of generous givers. Scientists are energized. Doctors, nurses and other caregivers are inspired. The effect is more than financial; it’s knowing that someone out there cares, that we are not alone, that someone understands and supports our commitment to the sick and injured. You can’t put a price on that feeling.

Donors themselves benefit in countless tangible and intangible ways. I was interested to hear of recent studies linking the donation of time or money to a variety of positive health indicators. Givers seem to have lower blood pressure, less depression and lower stress. In two studies, older people who volunteered experienced a 44 percent reduction in five-year mortality. The best reward, of course, is knowing that your gift may save a life, stop a disease and reduce the overall burden of suffering.

Cleveland Clinic recently launched a major philanthropic campaign, called “The Power of Every One.” The response has been overwhelming. Dynamic business and civic leaders have jumped on board to lead the effort. Their energy and commitment are inspiring.

We have some distance to go to meet our ambitious goal, but from what I’ve seen so far, the American tradition of exceptional philanthropy is alive and well. And that spirit of goodwill can help bridge the gap between what we can afford to do and what we desire to do.

Delos M. Cosgrove, MD
CEO and President
Cleveland Clinic
Be the One

Dear Friends,

Thank you for taking a few minutes to page through (or read cover to cover!) our latest edition of Lerner Research Institute Magazine. This publication is an opportunity for us to share with you some of the groundbreaking research going on in LRI and how it relates to you. We are proud to have lots of exciting stories to tell.

The theme of this issue and of our upcoming Friends of the LRI event in November is to highlight and gather support for our young investigators. These individuals are in the early stages of their research careers, a tenuous time in the life of a scientist. Securing financial support for new projects can be challenging, and many funding agencies are unwilling to provide support until significant data has been generated. So how does a young investigator get a new idea off and running? Enter philanthropy! Philanthropic dollars are often the catalyst to jump-start some of the most innovative projects.

Cleveland Clinic recently launched the public phase of a new and very ambitious campaign, called “The Power of Every One.” One of the cornerstones of this campaign is support for scientific research, which is paramount to Cleveland Clinic’s ability to provide exceptional patient care. Would you like to be “the ONE” who helps find a cure for a disease? “The ONE” who helps a young researcher get started on their path to discovery?

Yes, your philanthropic gift can be “the ONE” that will make a difference.

Philanthropic funding is often the bridge that takes a discovery from the laboratory to the bedside. I invite you to join me at this very exciting time to learn about these discoveries and help make potential cures a reality. Please contact me or my colleague, John Keller (kellerj@ccf.org, 216.445.6299), with any questions you may have, or allow us to give you a tour of our facilities. We know you that you will be amazed at what you see. John and I hope to see you soon.

My best,

Shawna Hofstetter
Senior Director of Development
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Every 40 seconds, someone in the United States has a stroke. Many of these individuals die, and those who survive often face a lifetime of disability. Stroke costs billions of dollars in healthcare services, medications and missed days of work. Yet, very few successful treatments have been found for what now is the fourth leading cause of death in the nation.

Selva Baltan, MD, PhD, of the Department of Neurosciences, hopes to change the trajectory of stroke research. “In the past decade, we have learned valuable lessons,” Dr. Baltan says. “We have improved our technology, experimental designs and analysis of our results for better translation of scientific discoveries into clinical trials.”

She explains that early stroke research focused on salvaging neurons, the principal cells of the brain. However, these compose only about half of the brain. The other half—known as “white matter”—consists of axons, which are the pathways or connecting cables that transmit messages between brain cells, and glia, which are specialized support cells. Without white matter, the brain cannot function, but very little is known about what happens to it during stroke.

Dr. Baltan is particularly interested in how age affects white matter in the context of stroke. As we age, axons begin losing their power and ability to transmit signals properly. This weakening of signals makes it much more difficult for elderly patients to recover from stroke. Dr. Baltan has discovered that two FDA-approved cancer drugs can help axons regain their strength to improve recovery after stroke or possibly to prevent stroke in those who are at high risk. Philanthropic support would help support clinical trials of these drugs. Because these drugs already are approved for human use, the time from clinical trial to widespread use could be quicker than it is for drugs that have not been approved.

Challenges facing stroke research, including reduced federal funding, have led many former stroke researchers to change their focus. Dr. Baltan remains dedicated to stroke research, advocating for federal funding and mentoring other stroke researchers. “The growth of our aging population places a large number of people at risk for stroke, and this creates a challenging gap that we must close,” she says. “This is an exciting time to support stroke research and inspire scientists to make new discoveries.”

Pictured: Selva Baltan, MD, PhD

Images courtesy of Dr. Selva Baltan
STROKE:  
4 Things You Need to Know

When it comes to stroke, it’s important to understand your risk and to work closely with your doctor. “It comes down to knowing your risk factors,” says stroke neurologist M. Shazam Hussain, MD. “Paying attention to your health can go a long way in protecting you against a stroke.”

Here are things about stroke you should know:

1. **Your age is the biggest risk factor**
   The biggest risk factor for stroke is age, traditionally over the age of 55 for men and 60 for women. But if you’re younger, don’t assume you’re in the clear. “We are seeing more and more young people with stroke,” says Dr. Hussain. “Don’t think that because you’re under a certain age, you are completely protected.”

2. **Some risks can be controlled**
   Some stroke risk factors are beyond your control, like family history — you’re at higher risk if a parent, grandparent, sister or brother has had a stroke or a heart attack at an early age. But some risk factors may be controlled, especially when you work closely with your doctor, Dr. Hussain says. “We work with people to watch their blood pressure and control cholesterol levels, and we encourage them to quit smoking, limit alcohol, eat healthy and exercise regularly. These are all powerful ways to lessen your risk,” he says, adding that while risk reduction is variable, it can be 50 percent or even greater.

3. **You can calculate your risk**
   There’s no shortage of opportunities for you to know and understand your risk of stroke, including stroke risk calculators that will give you a score based on your age, blood pressure, smoking habits and minimal medical history. But your best bet is to maintain a relationship with a primary care physician and keep up with regular physicals, where screening for stroke risk factors is standard.

4. **If you’ve already had a stroke, you need to be vigilant**
   “If a person has already suffered from a stroke or heart attack, we watch very closely for things that could put you at risk for another one,” says Dr. Hussain. He says doctors watch for stenosis — a narrowing of the blood vessels — especially in the carotid arteries that carry blood to the brain. They also monitor your heart rhythm to watch for atrial fibrillation, or an irregular heartbeat. They may recommend medications or surgery to reduce your risk of another stroke.

“Pictured: Dr. Baltan’s Stroke Research Team

“This is an exciting time to support stroke research and inspire scientists to make new discoveries.”

Courtesy of Cleveland Clinic Health Hub. Clevelandclinic.org/healthhub
Some of the most promising discoveries occur when scientific fields overlap, leading to the possibility of new treatments arising in unexpected ways.

Such is the case with recent research by Angela Ting, PhD, of the Genomic Medicine Institute, who applies epigenetics in her investigation of prostate cancer.

Because most prostate cancers are very slow growing, they may not warrant chemotherapy or radiation, especially in elderly men. For deadlier forms, however, immediate and aggressive treatment is required. Unfortunately, there still is no way of predicting who will develop lethal prostate cancer, making it difficult for physicians to know when they should prescribe costly and invasive treatments. Dr. Ting is developing new ways for physicians to quickly and accurately determine appropriate treatment based on the unique epigenetic profile of a patient’s cancer.

Dr. Ting describes epigenetics as the study of how genes are turned on and off in response to internal factors, such as hormone levels, and external, environmental factors, including diet and toxin exposure. Epigenetic patterns define how a gene functions in healthy cells. However, when these patterns become abnormal, they can lead to uncontrolled cell growth and cancer. Dr. Ting’s research centers on a specific pattern, DNA methylation, that is greatly altered in cancer. She recently discovered that prostate cancer patients have an unusually high level of DNA methylation in a specific gene, ABCA1, that normally regulates cholesterol’s transportation from cells. However, when this gene is turned off, cholesterol tends to build up inside the cells.

Excess cholesterol is a chemical precursor to male hormones, which prostate cancer cells need to survive. When their hormone supply is cut off, most prostate tumors die. However, when aggressive, lethal prostate tumors run out of hormones, they use cholesterol to make more.

In patients with altered ABCA1 and excess cholesterol in their cells, the gas tank is always full, which fuels cancer’s growth and spread. Dr. Ting is looking into whether the use of cholesterol-lowering drugs could increase survival of men with this gene alteration.

She has found that epigenetic changes in ABCA1 are present in up to 71 percent of aggressive prostate cancers, suggesting that a method of detecting or reversing the change could save thousands of lives each year. Her laboratory also is working on other targets they discovered to understand how these changes affect prostate cancer development and progression.

“Our goal is to develop a quick and easy urine test that shows changes when prostate cancer is in its earliest stages,” she explains. “Philanthropic support could help make this simple test a reality, which could save lives.” Dr. Ting also is applying her ideas to other diseases, including ovarian and colorectal cancer.
Kicking for the Dream

Cleveland Browns kicker Billy Cundiff, president of Colleen’s Dream Foundation, recently visited Lerner Research Institute and gave $20,000 to support the ovarian cancer research of Angela Ting, PhD.

The funds were raised through “Kicking for the Dream,” an online fundraising project Cundiff created to encourage kicking specialists from around the world to support ovarian cancer research. Cundiff and Browns punter Spencer Lanning raised more than $10,000, which was matched by Colleen’s Dream Foundation. “Both Spencer and I agreed it was important the money we raised should be kept in Cleveland to help grow the talent at Cleveland Clinic,” says Cundiff. “Cleveland Clinic is doing amazing work. And the ovarian cancer research they are conducting is very important in fighting this deadly disease.”

To learn more about how you can personally support life-changing research, contact Shawna Hofstetter, Senior Director of Development, at 216.445.8523 or hofstes@ccf.org.
The loss of an arm is a life-changing event, creating physical and psychological challenges. Recent advances have led to a new generation of robotic prosthetic limbs, which are connected to the body’s nervous system and allow patients to move their limbs simply by thinking about an action. These devices allow for movement of individual fingers and even bend at multiple joints, making them look and move more like a real arm.

However, prosthetic limbs are still missing a crucial element: the sense of touch. Without this, a person cannot accurately gauge the amount of force needed to shake someone’s hand, open a bottle or pick up an egg. Even the simplest action can be slow and difficult, as the person must closely watch the movement and placement of the prosthesis at all times. This makes multitasking nearly impossible. Paul Marasco, PhD, of the Department of Biomedical Engineering, is developing prosthetic devices that feel like a natural part of the body.

“If we can restore a patient’s ability to open and close a prosthetic hand without having to watch it, we have reached the holy grail,” he says.

Dr. Marasco works closely with patients at the Louis Stokes Cleveland Department of Veterans Affairs Medical Center (VAMC), which has a large population of patients who have had limbs amputated. His research combines laboratory data with patients’ personal experiences and suggestions to understand how the senses of limb movement are organized in the brain and how the brain changes and compensates for the loss of a limb.

Dr. Marasco also is applying his expertise to one of the largest healthcare problems in our society — diabetes. “The vast majority of lower-limb amputations are in diabetic patients,” he says.

Diabetes can cause nerve damage and poor blood circulation in the lower limbs, leading to a loss of sensation. Dr. Marasco is trying to better understand the cognitive effects that occur when these changes take place, and his early results are promising. Philanthropic support could help him bridge the gap between what patients think and how they “feel.”
70 thousand people a year will lose a lower limb to diabetes.

230,000 deaths each year.

1 in every 400 children will have it.

$245 billion to treat this disease.

90% of all diabetes found in the U.S is Type 2 diabetes.

Risk Factors:
- Increasing age
- A family history of diabetes
- Obesity
- Hypertension (high blood pressure)
- Race or ethnic background
- A history of gestational diabetes
- Smoking
- Prolonged & heavy alcohol consumption
- Use of certain drugs

Preventive Steps & Lifestyle Tips:
- Weight Loss
- Healthy diet
- Exercising
- Oral Medication
- Insulin injections if oral medication fails
- Bariatric surgery for obese people with diabetes
Inflammatory bowel disease (IBD) is a lifelong intestinal disorder with symptoms ranging from chronic cramping, bloating and diarrhea to rectal bleeding, anemia and malnutrition. Individuals with IBD often struggle to maintain normal, active lives, as disease symptoms can flare up at unpredictable times and result in pain, disability and embarrassing social situations. One type of IBD, Crohn’s disease, typically affects young people in their late teens and early 20s. Approximately 700,000 Americans have been diagnosed with Crohn’s disease, and that number continues to rise.

It is unclear why some people develop Crohn’s disease, but it appears that a combination of factors causes disease. Christine McDonald, PhD, of the Department of Pathobiology, is interested in determining how a person’s family history (genetics), the bacteria in their gut (microbiome) and the things they are exposed to (lifestyle) synergize to cause Crohn’s disease. “What is particularly concerning is the relatively recent, rapid increase in Crohn’s disease,” she says. “This rise points to something in our modern lifestyle that is promoting disease development.” One potential contributing factor, she believes, is the widespread use of food additives.

Maltodextrin (modified cornstarch), a common food additive used to improve flavor and texture in many packaged foods, appears to alter intestinal bacteria, making it very sticky, Dr. McDonald discovered. Another recent study from her lab showed that maltodextrin promotes survival of Salmonella bacteria, commonly associated with food poisoning. Her research indicates that maltodextrin can increase the amount of bacteria in the gut, as well as decrease a person’s anti-bacterial defenses, potentially creating an ideal environment for Crohn’s disease to develop.

Philanthropic support would help Dr. McDonald expand her lab’s studies to include patient populations.

“It is our hope that by understanding the complex interactions of these risk factors, especially ones that we can control, like diet, we can reduce Crohn’s disease,” she says.
Crohn’s and Colitis Foundation Funds New Research

Inflammatory bowel diseases (IBD), such as Crohn’s disease and ulcerative colitis, are chronic inflammatory disorders of the intestine, affecting more than 1.5 million people in America. Booki Min, DVM, PhD, Department of Immunology, recently received a three-year, $350K grant from the Crohn’s and Colitis Foundation to develop new methods to reduce inflammation and improve symptoms for patients with these debilitating diseases.

Our intestines are constantly exposed to foreign substances in the foods we eat and in our normal “gut” bacteria. Our bodies tolerate these substances because of suppressive mechanisms that calm our immune cells. When these suppressive mechanisms do not work properly, the immune cells attack the foreign invaders, leading to uncontrolled inflammation in the intestines. One of these suppressive mechanisms involves specialized immune cells called regulatory T cells (Tregs). Dr. Min has discovered an essential pathway that activates Treg function and ensures that the Tregs work properly to suppress inflammation. With this new funding from the Crohn’s and Colitis Foundation, his team will be able to delve deeper into how this pathway works and possibly develop a novel Treg-based immune therapy.

Cleveland Clinic has an international reputation for excellence in treating inflammatory bowel disease (IBD). Here we take a look at why IBD expertise is critical to patients and at our volumes and outcomes.

**People in U.S. Affected by Crohn’s and Ulcerative Colitis**

1 in 200

**Number of Genes** identified to date associated with IBD. Researchers at Cleveland Clinic co-authored the paper in which the first gene associated with Crohn’s disease (NOD2) was identified.

163

**About 35-40%** of Crohn’s disease patients may require a reoperation every five years because of the disease’s recurrent and complex pathology.

OF PATIENTS WITH ULCEERATIVE COLITIS MAY NEED SURGERY IN THEIR LIFETIME.
The herpes virus family is best known for causing diseases like chickenpox, shingles, and mononucleosis. But a relatively unknown member of the same family, human cytomegalovirus (HCMV), infects 80 percent of people by the time they reach the age of 40 and can cause severe illness, organ complications and death. So why haven’t we heard about this virus?

Pictured: Eain Murphy, PhD
Initial infection with HCMV causes mild symptoms that can be confused with the common cold or flu, and the virus then goes dormant. In individuals with healthy immune systems, the virus is likely to continue sleeping, and those individuals may never know that they are infected. HCMV becomes problematic, however, when it is reactivated.

In patients with compromised immune systems, including the elderly, pregnant women and bone marrow recipients, reactivation of HCMV poses a real threat. Unfortunately, there is no vaccine, and available drugs often are poorly tolerated and ineffective. Eain Murphy, PhD, of the Department of Molecular Genetics, is working to understand the process of HCMV reactivation and develop new methods to prevent it. He developed a new technique to visualize the process of reactivation so that it can be better understood. With this method, HCMV-infected cells appear red when viewed under a microscope, but when the virus begins reactivating, a chemical process makes it appear green. Using this technique, Dr. Murphy tested the effectiveness of 3,480 existing drugs and found 42 of them inhibit the virus from reactivating. He now is collaborating with researchers at Princeton University on a large-scale screening of 250,000 additional drug compounds.

Philanthropic support would allow Dr. Murphy to test his drug candidates in various groups of patients at risk of developing serious illness from HCMV. He developed the first model to study HCMV in donated bone marrow cells, a common reservoir for the virus.

“Sixteen percent of bone marrow recipients get HCMV,” Dr. Murphy says. “Our goal is to be able to treat donated marrow with drugs so that the virus never wakes up.”

With support from generous benefactors, Dr. Murphy could take his research from the lab bench to the bedside in only a few years.

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**Are You at Risk for HCMV?**

These four groups are at risk for HCMV complications.

**Newborns**

1:150 children are born with HCMV.

**Immunosuppressed patients**

Chemotherapy patients and bone marrow transplant recipients’ immune systems cannot effectively fight the virus.

**Immunocompromised patients**

The elderly and AIDS patients are more susceptible to HCMV complications.

**Patients with age-related diseases**

HCMV is more likely to reactivate in patients with clogged arteries or certain types of cancer.
A Lerner Research Institute researcher has made a discovery that could lead to new drugs to prevent or treat obesity — and the diseases that come with it. J. Mark Brown, PhD, of the Department of Cellular and Molecular Medicine, successfully prevented obesity, type 2 diabetes and liver damage in a lab study in which mice were fed a high-fat diet, a known risk factor. While researching a rare mutation of the gene ABHD5, which alters how the body stores fat, Dr. Brown stumbled across its cousin: ABHD6, instrumental in regulating appetite.

ABHD6 is part of a system that modulates functions such as appetite, mood and pain. Previous studies have shown that blocking this system can reduce obesity. But doing so comes with serious side effects, including anxiety, depression and suicidal thoughts. ABHD6, however, might provide an alternative. It exists throughout the body, not just in the brain. Dr. Brown set out to block ABHD6 in a peripheral area, the liver, to see if he could prevent obesity without triggering side effects.

After 12 weeks, the result was a “striking metabolic outcome,” Dr. Brown says. Lab study subjects did not gain weight or develop type 2 diabetes or liver disease — and they were more active. The next step is developing a phase I trial in humans. “We still have a lot of biology to understand. We don’t know how ABHD6 impacts the central nervous system or how the brain is signaling the animals to move around more,” he says. Little was previously known about ABHD6, so the discovery is promising, Dr. Brown says. “We have a unique stake in the ground.”

Originally published in Cleveland Clinic Catalyst magazine.
Keeping off those extra pounds is an ongoing battle for many women. And it only gets more challenging as we enter menopause. It’s just the way we’re made. Female hormones tend to promote fat formation. That means our bodies store fat more easily than men’s bodies. As we get older, our metabolism slows, enabling even more weight gain. And as we lose muscle mass (beginning at age 40), body fat often takes its place. As we age, we need to do more to combat these changes.

Why not let nature take its course? Because being overweight — at any age — generally means you have higher cholesterol and higher blood pressure. These increase your risk for a variety of diseases, including this biggie: diabetes.

**Prediabetes: precursor of diabetes**

Prediabetes occurs when your blood glucose levels are higher than normal — but not yet high enough to be diabetes. Still, your risk of heart attack is 1.5 times higher than normal. (It’s two to four times higher with diabetes.) And long-term cardiovascular damage may already be happening.

According to the American Diabetes Association, people who develop type 2 diabetes almost always have prediabetes first. Without preventive measures, prediabetes can become full-blown type 2 diabetes in three to 10 years. This doesn’t always have to happen. Not when prediabetes is viewed as a wake-up call for adopting a healthier lifestyle.

Many people can prevent diabetes — even if they have a family history of the disease. Maintaining a normal body weight is key.

**Why you need a blood sugar test**

To protect yourself from developing type 2 diabetes or prediabetes, get a blood test. Blood sugar tests are as important for mid-life women as regular mammograms and bone density screenings.

Prediabetes is diagnosed from a blood test when:

- Hemoglobin A1c levels are 5.7 to 6.4 percent
- Fasting blood sugar is 100 to 125
- Two-hour glucose is 140 to 199 after a glucose challenge

Have a blood test every three years, starting at age 45, so you can track your scores and offset any warning signs of diabetes right away. Start earlier if you:

- Have a family history of diabetes
- Have high blood pressure or high cholesterol
- Had gestational diabetes
- Gave birth to a baby weighing more than 9 pounds

*Courtesy of Cleveland Clinic Health Hub*  
*Clevelandclinic.org/healthhub*
Plan Now to Secure the Future

TESTAMENTARY GIFTS

Americans are able to make decisions about the distribution of their assets for their lifetimes and beyond through charitable giving and taking advantage of income-tax deductions and estate-tax savings. By planning now, you can provide for the future of Cleveland Clinic and the Lerner Research Institute through your will and testamentary designations.

There are many reasons for making a testamentary charitable gift, with various benefits. At a young age, between 40 and 60, individuals still are working, saving for retirement and even supporting college education for children or grandchildren. At this age, they might be hesitant to make a large gift with assets that might be needed in the future. Similarly, individuals between ages 60 and 75 may be newly retired or planning for retirement and beginning to make financial and charitable plans for the future. All may wish to make a meaningful gift, but are concerned about making that commitment just yet. By including a charitable gift in a will, or by making Cleveland Clinic the beneficiary of a life insurance policy or a retirement plan, a gift can be established now without adversely affecting the future.

Federal Estate Tax Exemption

In adherence to the American Taxpayer Relief Act of 2012 (ATRA), the 2014 estate-tax exclusion is $5.34 million. Anything exceeding that amount will be taxed at 40 percent, which is up from 35 percent in 2013. Any unused exemption when a spouse passes away may be carried over to the surviving spouse. Therefore, a married couple can pass along up to $10.68 million free of any federal estate tax.

Avoiding estate tax often may not be the primary motivation for giving. With the estate-tax exemption now at $5.34 million, few individuals are making a bequest only to lessen their estate tax burden. Other motivations include a strong relationship with an organization, identifying with that community, an association through volunteer work, passionate personal beliefs, a sense of satisfaction from helping a worthy cause and the ability to further personal and charitable goals.

Testamentary gifts have become an integral part of our American philanthropic tradition, and our tax laws encourage charitable support. With financial and estate planning, you can support Cleveland Clinic’s research and medical excellence and benefit future patients while also securing your family’s financial future.

To learn more about how you can personally support life-changing research, contact Shawna Hofstetter, Senior Director of Development, at 216.445.8523 or hofstes@ccf.org.
Chair’s Innovative Research Fund

A lagging federal research budget has led many scientists to put their more innovative projects on hold and focus on proven experiments that have a higher chance of receiving funding. The Lerner Research Institute Chair’s Innovative Research Fund was established in 2011 to help overcome these challenges. Designed by Paul E. DiCorleto, PhD, holder of the Sherwin-Page Chair, the program encourages investigators to pursue creative research by providing $50,000 for one year (renewable for a second year) to help them gather enough preliminary data to submit a competitive federal grant proposal.

Forty investigators applied for Innovative Research funding in 2014, and two projects were chosen.

Kathleen Derwin, PhD, of the Department of Biomedical Engineering, will study a method to restore muscle volume in patients with traumatic injuries caused by major muscle loss or damage, such as combat injuries. Her research will focus on a specific protein that has been found to increase muscle mass in laboratory experiments. Her long-term goal is to develop regenerative medicine strategies for restoring functional muscle tissue.

Thomas McIntyre, PhD, of the Department of Cellular and Molecular Medicine, will investigate how the activation of platelets — cellular fragments that are involved in the formation of blood clots — leads to the development of cardiovascular disease. In particular, he will study the effects of a new stimulator of platelet function and potential drug candidates that could prevent the formation of dangerous blood clots.
Meet our Newest Staff Members

The Lerner Research Institute welcomes six new staff members, each of whom offers unique skills and expertise to enhance our disease-focused research programs.

Lynn M. Bekris, PhD, was recruited to the Genomic Medicine Institute from the University of Washington, Seattle, where she was a Research Assistant Professor in the Department of Medicine, Division of Gerontology and Geriatric Medicine. She brings expertise in the discovery of genetic biomarkers in Alzheimer’s and Parkinson’s disease and other dementias. She obtained her PhD in toxicology from the University of Washington.

Jarrod Dalton, PhD, a Cleveland Clinic caregiver since 2006, was promoted in 2014 to Assistant Staff, Quantitative Health Sciences. He obtained his PhD in epidemiology and biostatistics from Case Western Reserve University; his earlier degrees were in mathematics, computer science, business and applied statistics. With special interest in medical decision making and in clinical prediction models, he has coauthored publications on clinical outcomes in journals of the anesthesiology, pain control, and critical care disciplines and in Statistics in Medicine. Dr. Dalton was recently awarded funding via the NIH KL2 (Mentored Career Development Award) program.

Angelika Erwin, MD, PhD, is an expert in adult metabolic disorders. She comes to the Genomic Medicine Institute from the Department of Genetics and Genomic Sciences, Mt. Sinai School of Medicine, New York, and brings combined expertise in internal medicine and medical genetics. Dr. Erwin received her PhD (magna cum laude) from Eberhard-Karls University in Tübingen, Germany, and her MD from Humboldt University’s Medical School (Charité), Berlin, Germany.
Tomas Radivoyevitch, PhD, joined the Department of Quantitative Health Sciences from Case Western Reserve University's Department of Epidemiology and Biostatistics, where he was an assistant professor for the past 14 years. He received dual master's degrees in chemistry and systems engineering from CWRU and a PhD in environmental risk assessment from the Medical University of South Carolina. Dr. Radivoyevitch provides statistical analysis support to Taussig Cancer Institute researchers and pursues research in treatment-induced leukemia and related disorders.

Jeevanantham Rajeswaran, PhD, is a newly appointed assistant staff member in the Department of Quantitative Health Sciences (QHS). Dr. Rajeswaran is a former lead biostatistician in QHS and recently received a PhD in biostatistics from Case Western Reserve University. His research focus is on cardiovascular outcomes, and he works closely with investigators in the Miller Family Heart and Vascular Institute on research study design and statistical analysis.

Kwai Ping (Connie) Tam, PhD, joined the Departments of Ophthalmic Research and Molecular Genetics from the University of California, Berkeley. Her PhD in biochemistry is from Hong Kong University of Science and Technology; previous degrees were in chemical engineering (magna cum laude) and biotechnology. Her research concerns the cornea's defenses against the eye condition keratitis and has worked on shufflons (inverted DNA segments) in Salmonella infection. She has coauthored reports in the Journal of Clinical Investigation and others and has NIH funding to investigate bacterial keratitis.
New Endowed Chair

Paul L. Fox, PhD, a longtime staff member in Cellular and Molecular Medicine and holder of the Robert Canova Endowed Chair in Inflammation Research, has established the Paul L. Fox, PhD, Endowed Chair in Molecular Medicine at the Lerner Research Institute to help advance the understanding of molecular mechanisms that underlie disease.

The first Fox Chair holder is Xiaoxia Li, PhD, of the Department of Immunology. Dr. Li is an international expert who has published extensively on the biological pathways of inflammation, which applies to multiple disease areas. Her ultimate goal is to develop new drugs to treat diseases of the immune system. “This endowed chair will allow my laboratory to engage in exciting research to better understand and treat autoimmune and inflammatory diseases,” says Dr. Li. “At a time when diminished funding from federal agencies has constrained the progress of research nationwide, this generous gift will help to accelerate the pace of discovery.”

This endowment marks the first time in LRI’s history that a staff member has given back so generously to support fellow scientists. “I know first-hand how valuable an endowed chair is to a research program because I was honored a few years ago by receipt of the Robert Canova Endowed Chair in Inflammation Research,” says Dr. Fox. “An endowed chair is much more than just an honor — its support has enabled my laboratory to take exciting and risky new directions that we otherwise could not explore. Personally, I am honored that Dr. Xiaoxia Li has been named as the first recipient. Not only is Dr. Li an exceptionally innovative scientist, she is a friend, colleague and collaborator, and I can’t think of anyone more deserving of this Chair.”

The Fox Chair was established as part of Lerner Research Institute’s Endowed Chair Challenge, in which Cleveland Clinic provides $1 million in matching funds. Endowed chair holders may use the funds to start new projects, support additional staff, pay for equipment, and cover the cost of obtaining preliminary data for future grant applications.

For more information about the Endowed Chair Challenge, please contact Shawna Hofstetter, Senior Director of Development, at 216.445.8523 or hofstes@ccf.org.

Pictured: Xiaoxia Li, PhD, and Paul L. Fox, PhD
A research team led by Paul Fox, PhD, of the Department of Cellular and Molecular Medicine and holder of the Robert Canova Endowed Chair in Inflammation Research, has discovered a new form of a widely studied protein involved in the growth and spread of cancer.

Blood provides tumors with nutrients and oxygen they need to survive, expand, and migrate to other parts of the body. As such, finding a way to stop the formation of new blood vessels, called angiogenesis, is a major area of study in cancer research. Specifically, a protein called VEGF-A, which is known to be a principal driver of angiogenesis, has been heavily studied and is the target of several current anti-cancer drugs.

Remarkably, Dr. Fox’s lab discovered a new form of VEGF-A, which they call VEGF-Ax, that actually decreases angiogenesis and inhibits the growth and spread of cancer. The team found that VEGF-Ax is formed when the cellular machinery that builds proteins reads through its genetic stop sign and adds 22 additional amino acids to VEGF-A. “It is truly remarkable that a small change in a protein sequence leads not just to a protein with a different function, but one with a function completely opposite to the original,” says Dr. Fox. “In the context of cancer, the small extension changes a very “bad” protein into a very “good” one.”

This discovery, reported in the high-impact journal Cell, will likely open new avenues of angiogenesis and cancer research. It may also have implications for current and future cancer treatment strategies.
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