

THE HARRINGTON PROJECT
FOR DISCOVERY & DEVELOPMENT

Harrington Discovery Institute

 University Hospitals | Cleveland Ohio



MOMENTUM
MOVING MEDICINE FORWARD:
2015 – 2016 Harrington Discovery Institute Annual Publication

Dear Colleagues,

Four years ago the Harrington family made the decision to establish The Harrington Project for Discovery & Development with the goal of accelerating breakthrough discoveries into medicines. How quickly we have gathered momentum!

Today, The Harrington Project is being recognized as a novel paradigm for accelerating academic discoveries into medicines, and we are on a continued growth trajectory. In launching our fourth class of Harrington Scholar-Innovators, we will have evaluated more than 1,500 discoveries and supported about 60 programs across the United States and United Kingdom. We have solidified relationships with Alzheimer's Drug Discovery Foundation and Foundation Fighting Blindness, strengthened our ties with University of Oxford in the United Kingdom and together with BioMotiv, the for-profit, mission-aligned accelerator, successfully partnered with several pharmaceutical companies.

Annually, Harrington Discovery Institute supports 35 scholar projects. Our Innovation Support Center, which oversees the development of these programs, has gained recognition in the physician-scientist community as a truly differentiating capability. Several Harrington Scholar-Innovator projects have transitioned this year to BioMotiv, bringing BioMotiv's portfolio to eight. Three discoveries have been licensed to major pharmaceutical companies. The Harrington Prize for Innovation in Medicine, the product of our collaboration with the American Society for Clinical Investigation, is attracting exceptional nominees from across the globe and is increasingly identified with innovation, creativity and clinical impact at the highest level.

Sincerely,



Jonathan S. Stamler, MD

President, Harrington Discovery Institute

Robert S. and Sylvia K. Reitman Family Foundation

Distinguished Chair in Cardiovascular Innovation

Director, Institute for Transformative Molecular Medicine

Professor of Medicine and Biochemistry, Case Western Reserve University School of Medicine

We have invested significantly in our infrastructure by recruiting outstanding leaders to join our team. Mukesh K. Jain, MD, an internationally renowned physician-scientist, is making his mark as our Chief Scientific Officer. Shobha Parthasarathi, PhD, Director, Strategic Initiatives, and Diana R. Wetmore, PhD, Director, Innovation Support Center, combine solid industry experience with a keen understanding of our mission and vision. We have instituted an Investment Advisory Board of eminent investors and entrepreneurs to act as an investment committee, thereby ensuring financial stewardship of our nonprofit Harrington Discovery Institute.

With these valuable additions to our leadership, Harrington Discovery Institute is positioned for continued growth and new initiatives. Over the next year, we plan to test the concept of Centers of Excellence in specific clinical areas linked with our foundation partners. The Centers of Excellence will be hubs of discovery and translational research, focused on science and innovation and aligned with philanthropy. We will continue to carefully select opportunities that are consistent with our model and mission.

Thank you for embracing our vision and your willingness to walk with us through the next phase of Harrington Discovery Institute's development. We believe that the institute's potential to impact human health is coming into sight.



On cover, Innovation Support Center Advisory Panel members Lawrence S. Olanoff, MD, PhD, (top right) and George Trainor, PhD, (bottom left) meet with 2015 Harrington Scholar-Innovator Geoffrey S. Pitt, MD, PhD, at Harrington Discovery Institute's Fourth Annual Scientific Symposium. Dr. Olanoff's interview can be found on page 11.

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HARRINGTON DISCOVERY INSTITUTE **MISSION:**

To advance medicine and society by enabling inventive physician-scientists to turn their discoveries into medicines that improve human health.

FIVE Good Minutes

with **Mukesh K. Jain, MD, FAHA**

*Chief Scientific Officer,
Harrington Discovery Institute
and Chief Scientific Officer,
University Hospitals*

Mukesh K. Jain, MD, FAHA, is Chief Scientific Officer of Harrington Discovery Institute and Chief Scientific Officer for University Hospitals. He is internationally recognized for studies that established a central role for a specific family of genetic factors termed Kruppel-like factors (KLFs) in cardiovascular biology, innate immunity and metabolism. Dr. Jain's clinical and academic contributions are recognized by numerous awards and honors, including election to the American Society for Clinical Investigation (ASCI), of which he is immediate past-President; Association of American Physicians; and Association of University Cardiologists.

Here, Dr. Jain shares his passion for the physician-scientist and Harrington Discovery Institute's model for drug development.



WHAT ARE YOUR RESPONSIBILITIES AS CHIEF SCIENTIFIC OFFICER OF HARRINGTON DISCOVERY INSTITUTE?

I have four primary responsibilities. First, I serve as “gatekeeper” for entry into Harrington Discovery Institute, providing scientific oversight for all award programs. This includes our signature Scholar-Innovator program as well as our foundation scholar partnerships and Oxford-Harrington Programme.

Second, I oversee selection of the annual Harrington Prize for Innovation in Medicine recipient. This program began in 2014 when I was a member of the leadership team for the American Society for Clinical Investigation. It is very gratifying to see the number of exceptional physician-scientists from around the globe who compete annually for this important recognition.

Third, I am responsible for organizing the Harrington Scientific Symposium, an annual event that showcases the work of our scholars.

Finally, I spearhead efforts to recruit outstanding physician-scientists to enrich our local community.

HARRINGTON DISCOVERY INSTITUTE IS DEDICATED TO ADVANCING THE WORK OF PHYSICIAN-SCIENTISTS. WHAT ARE THE CHALLENGES INHERENT IN THAT GOAL?

Physician-scientists are uniquely positioned to bridge the gap between clinical medicine and bench research. It is a core aspiration of such individuals to move fundamental discovery from the bench to bedside to impact human health. This translation of research discoveries is a decidedly nontrivial undertaking, one that most physician-scientists are not trained or well-positioned to accomplish. Further, most funding agencies support discovery-based research but do not support translation. Harrington Discovery Institute fills this critical gap by providing funding and drug development expertise to help physician-scientists fulfill this core aspiration.

WHAT IS THE PHYSICIAN-SCIENTIST'S ROLE TODAY?

Physician-scientists have several major roles. First, we have an obligation to deliver excellent clinical care. Second, we are invested in discovery and the translation of that knowledge to impact human health. Third, we serve as mentors to trainees who will hopefully become the next generation of scientists and physician-scientists. Fourth, we serve as educators of the medical students and leaders who shape American medicine.

WHY DOES HARRINGTON DISCOVERY INSTITUTE SUPPORT PHYSICIAN-SCIENTISTS AT MULTIPLE INSTITUTIONS?

Harrington Discovery Institute supports physician-scientists from institutions across the country who are carefully selected for the high quality and potential of their research. The fact is that no one institution can generate the 10 highest-quality projects in translational medicine on an annual basis. Thus, we felt it best to draw from a larger pool – i.e., the entire nation!

Our experience over the past four years since inception has affirmed the importance of this approach. Our scholars are truly exceptional individuals who have enjoyed and benefited from the significant financial resources and unparalleled drug development support provided by Harrington Discovery Institute.

WHAT CRITERIA ARE APPLIED TO SELECTING HARRINGTON SCHOLARS?

We seek accomplished investigators pursuing science of the highest quality with a therapeutic agent that has real potential to impact a specific disease condition. Each proposal undergoes both a rigorous scientific and drug development assessment. Once awarded, our team's efforts are focused on working with each scholar to advance their program to a level of maturity where commercial potential can be realized to the benefit of patients.

THE HARRINGTON PRIZE FOR INNOVATION IN MEDICINE

The Harrington Prize for Innovation in Medicine, established in 2014 by Harrington Discovery Institute and the American Society for Clinical Investigation (ASCI), honors a physician-scientist who has moved science forward with achievements notable for innovation, creativity and potential for clinical application.



Jeffrey M. Friedman, MD, PhD, Marilyn M. Simpson Professor and Director, Starr Center for Human Genetics, The Rockefeller University, and Investigator, Howard Hughes Medical Institute, is the recipient of the 2016 Harrington Prize for Innovation in Medicine for his discovery of leptin and the leptin-mediated pathway that controls feeding behavior.

2016 RECIPIENT OF THE HARRINGTON PRIZE
FOR INNOVATION IN MEDICINE

Jeffrey M. Friedman, MD, PhD

Jeffrey M. Friedman, MD, PhD, achieved international recognition for his 1994 discovery of leptin, a hormone that regulates appetite and body weight. In the laboratory, Dr. Friedman was able to isolate the gene that encodes for leptin and showed that the release of leptin by fat cells controls food intake and body weight.

In 2009, Dr. Friedman shared the prestigious Shaw Prize in Life Science and Medicine with Douglas Coleman, PhD, in recognition of their work. Prior to Dr. Friedman's discovery of leptin, Dr. Coleman used cross circulation experiments to predict that the ob gene encoded a hormone that regulated weight, although its identity was unknown prior to Dr. Friedman's work. The Shaw Prize is an international award that honors individuals who are currently active in their fields and have recently achieved distinguished and significant advances. In 2010, Dr. Coleman and Dr. Friedman also shared the Albert Lasker Basic Medical Research Award for their groundbreaking research.

Dr. Friedman's discovery of leptin and its role in regulating eating and obesity revolutionized medical and scientific thinking in this area. Based on the scientific evidence, Dr. Friedman postulated that many obese individuals suffer from a metabolic imbalance, caused by disruption of leptin's actions on neural circuits in the brain that control appetite and many other physiologic functions.

His fascination with leptin has persisted for more than 20 years. "Leptin and how it influences behavior has provided a molecular entry point for studying behavior," he says.

Dr. Friedman's latest investigations focus on the molecular mechanisms underlying leptin production and the role of nerve cells in food intake and body weight. In these studies, Dr. Friedman and colleagues are employing a new method they developed that enables the control of neural activity using magnets or radiowaves. He and his research team also are investigating the genetic basis of obesity with Turkish investigators, seeking to identify DNA mutations that contribute to differences in weight.

Yet many questions surrounding eating and its regulation remain unanswered, Dr. Friedman notes. "Eating is a very complex behavior. We still do not know even where the decision to eat is made," he explains.

Dr. Friedman's distinguished career in research had an unprepossessing beginning. At age 25, he was completing his internal medicine residency and missed the deadline for a GI fellowship at Boston's respected Brigham and Women's Hospital. Facing a gap year with no real plans, he was persuaded by John Balint, MD, chief of GI at Brigham at the time, to try laboratory research.

"It turned out I sort of liked research," Dr. Friedman recalls. "But I still wasn't ready to give up my medical training. I had done it for seven years and it took me a while to start feeling like a scientist rather than a physician."

In 1986, he relocated to The Rockefeller University and established his own lab. Less than 10 years later, Dr. Friedman made his trailblazing discovery. Since then he has received more than two dozen honors and awards, including international awards and induction into ASCI.

As the 2016 Harrington Prize winner, Dr. Friedman notes two aspects of the prize are of highest significance to him. "First, there is the deliberate connection to clinical medicine and translational research," he notes. "Second, it is coupled with the Harrington Symposium, an annual meeting of physician-scientists that is an opportunity to share with like-minded individuals."

In his Lasker Prize address, Dr. Friedman compared the experience of his original discovery with other significant life moments. "The only moments in my life that compared to this were when I was married and when I heard my twin daughters cry for the first time as they were delivered," he said.

Now, looking to the future, he shares what he considers the most-telling metric for success. "The best way to be remembered is that future generations know the work, whether or not they know who did it," he states. "That's what I would want."

Harrington Discovery Institute's "Secret Sauce"

The Innovation Support Center, an integral part of Harrington Discovery Institute, provides drug development expertise to enable Harrington Scholars to effectively and efficiently accelerate development of their discoveries into new therapies that impact patients' lives.

Under the leadership of Director Diana Wetmore, PhD, and Chairman Perry Molinoff, MD, the Innovation Support Center Advisory Panel advisors share their expertise with scholars in crucial areas of drug product development to enhance each project's potential for commercial success. Panel members have held senior management positions in national and international pharmaceutical companies,

and they have broad and deeply established business networks in the industry.

Each Harrington Scholar has access to all members of the panel with one member serving as a project-specific mentor and liaison. This lead strategic advisor calls on their panel colleagues to meet the individualized needs of each Harrington Scholar, thereby creating a custom "product development team" for each project.

Working with their lead strategic advisor, scholars develop a project plan targeting a clear commercial milestone. Panel members participate in project team meetings and are available for individual meetings and calls with scholars. Panel members also identify and access resources as needed for specialized expertise in areas such as intellectual property law, toxicology or regulatory strategy.



"I got the bug!" she explains. "I joined the company when I was 'in diapers' and stayed for 25 years. What kept me in industry was the incredible talent of our cross-disciplinary scientists, the wide variety of our R&D projects and the selflessness of our team work. We drove our projects in the fast lane; we lived with them 24/7." Dr. Debouck left GSK in 2008 to launch Ardennes.

Her broad and deep experience prepared her well for her role with the Innovation Support Center. "I can apply my expertise to all therapeutic areas and all different phases of drug discovery and development," she comments.

Dr. Debouck recently began working with 2016 Harrington Scholar-Innovator Ann Marie Schmidt, MD, (see page 28 for more information about Dr. Schmidt's work) and is wrapping up two years of dedicated work supporting 2014 Harrington Scholar-Innovators, including Rahul Kohli, MD, PhD, University of Pennsylvania, and Gavril Pasternak, MD, PhD, Memorial Sloan-Kettering Cancer Center.

Her interactions with Dr. Kohli illustrate how Innovation Support Center experts mentor Harrington Scholars.

Dr. Kohli, an infectious disease specialist, is studying a molecular pathway that leads to rapid antibiotic resistance with the goal of blocking the pathway to prevent resistance. Bacterial genetics is Dr. Debouck's specialty, and she describes

their pairing as "a perfect match." In addition to Dr. Debouck, Innovation Support Center Strategic Advisor George Trainor, PhD, a medicinal chemist, has been consulting on this project.

The team discussed the project in monthly teleconferences or in-person meetings at the University of Pennsylvania. "It was a very early project when we started two years ago," Dr. Debouck recalls. "We have been able to guide Dr. Kohli in his project and have assisted him in obtaining some additional funding from Harrington Discovery Institute. His project is now at the lead optimization phase."

The three scientists were not acquainted when they began meeting. "It was like an arranged marriage – we met, and we had to make it work," Dr. Debouck says. "It has been very collegial."

As the Innovation Support Center's relationship with Dr. Kohli winds down, Dr. Debouck reflects on their work together, stressing that the benefits of the mentoring relationship go both ways. "Working with the Innovation Support Center and the scholars allows me to participate in amazing research and help accelerate its path," she says. "And on the personal side, I feel as though I have made new friends."



LAWRENCE S. OLANOFF, MD, PHD

Innovation Support Center Advisory Panel member Lawrence Olanoff, MD, PhD, describes himself as a medicinal jack of all trades, master of none. His long career in the pharmaceutical industry gave him experience that is invaluable in his role as an advisor and mentor to Harrington Scholars.

Former President and Chief Operating Officer of Forest Laboratories, Inc. and now Special Advisor to the President for Corporate Relations at Medical University of South Carolina, Dr. Olanoff has created a lasting imprint on medical treatment in the United States. During his more than 30 years in the pharma industry, he was involved in the approval of some 30 new drugs, new indications or novel formulations. He currently serves on two corporate boards and numerous nonprofit boards, and he is actively involved in advising companies and nonprofit institutions in areas of drug discovery and development.

Dr. Olanoff explains his involvement with the Innovation Support Center. "I am intrigued with the concept of identifying the unique talent and innovations offered by academic physician drug discoverers," he says. "My objective is to find practical ways to assist them in taking the necessary 'next steps' to make their therapeutic approaches attractive to potential partners who can then thoroughly test the concept potentially all the way through clinical trials."

Dr. Olanoff earned a medical degree and a doctorate in biomedical engineering in the combined degree program at Case Western Reserve University School of Medicine in 1981. Those six years helped shape his career.

"I planned to devote my career to research," he recalls. "As I got more involved in my research, I decided my best career path was in the pharmaceutical industry, especially in the design and analysis of clinical studies."

Dr. Olanoff's particular specialty is clinical pharmacology. Since joining the Innovation Support Center Advisory Panel in 2014, he has worked closely with several scholars. Irina Petrache, MD, 2014 Harrington Scholar-Innovator, National Jewish Health in Denver, Colorado, is developing a novel treatment for chronic obstructive pulmonary disease (COPD) such as emphysema. (See page 61 for more information about Dr. Petrache's work.) Geoffrey Pitt, MD, PhD, Duke University, and David Clemmons, MD,

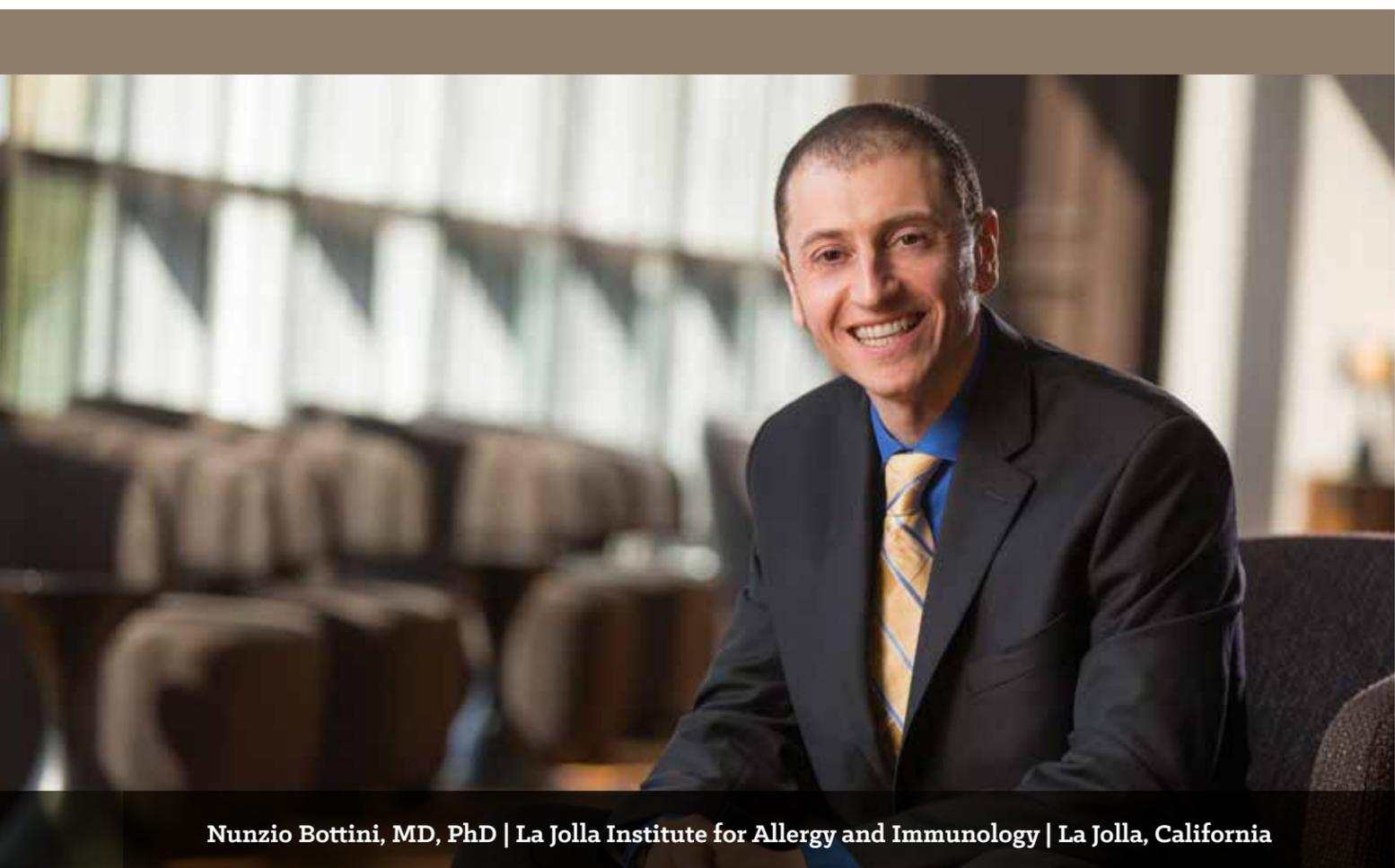
University of North Carolina, 2015 Harrington Scholar-Innovator, are developing different novel therapies for osteoporosis. Most recently, he has taken on the coordinator role for Benjamin Gaston, MD, Case Western Reserve University, a 2016 Harrington Scholar-Innovator, who is developing a treatment for respiratory depression (see page 16 for more information about Dr. Gaston's work).

"My role as a clinical pharmacologist is to determine whether a drug targets the disease in a meaningful manner, is it safe, does it have a good risk-benefit profile and the appropriate formulation, administration route and pharmacokinetic profile that will make it successful in the marketplace," Dr. Olanoff explains. "The question we are trying to answer at this stage is whether we translate this compound to a drug that patients will take and derive a benefit."

Although the Harrington model is still in its early stages, based on the experience of Harrington Scholars and Innovation Support Center mentors thus far, it appears Harrington Discovery Institute got it right.

Harrington Scholar-Innovator Program

Harrington Scholar-Innovators are physician-scientists chosen from institutions across the U.S. through a competitive selection process who receive funding and drug development support from Harrington Discovery Institute to advance their research toward clinical impact.



Nunzio Bottini, MD, PhD | La Jolla Institute for Allergy and Immunology | La Jolla, California

CURIOSITY Pays Off

Nunzio Bottini, MD, PhD, Associate Professor of Cellular Biology at the La Jolla Institute for Allergy and Immunology and consulting rheumatologist at the University of California, San Diego (UCSD), was born curious. It's part of the makeup of a physician-scientist, he says.

"Physician-scientists view disease as a problem that should be solved," Dr. Bottini explains. "Curiosity tells you there is a better way to treat these problems. As a scientist you can contribute to that."

In Dr. Bottini's case, curiosity has defined his career. After completing his MD and PhD at the University of Rome in his native Italy, Dr. Bottini received postdoctoral research training in biochemistry and signal transduction at the Sanford-Burnham Medical Research Institute in La Jolla, California. That experience ignited his interest in immunology, and he spent his first years in the United States in the laboratory.

Relocating to La Jolla Institute in 2009, Dr. Bottini's interest in immunology led him to rheumatology and autoimmune diseases, and he moved into the clinical sphere as well. With a keen understanding of signaling mechanisms in immune cells, he enjoys putting that training into practice with his patients.

"Rheumatology is very brainy in terms of how you proceed," he notes. "On the clinical side, there is a lot of thinking and science involved in a diagnosis. In terms of science in the lab, there is a lot you can do."

In rheumatoid arthritis, immune cells move into the joint and release antibodies that irritate local joint-lining cells, which amplifies pain and joint damage. For about one-third of patients, the drugs used to suppress the immune system are not effective, Dr. Bottini says.

"We want to develop a first-in-class drug for rheumatoid arthritis that complements current immune-targeted medications and does not increase the risk of infection," he states.

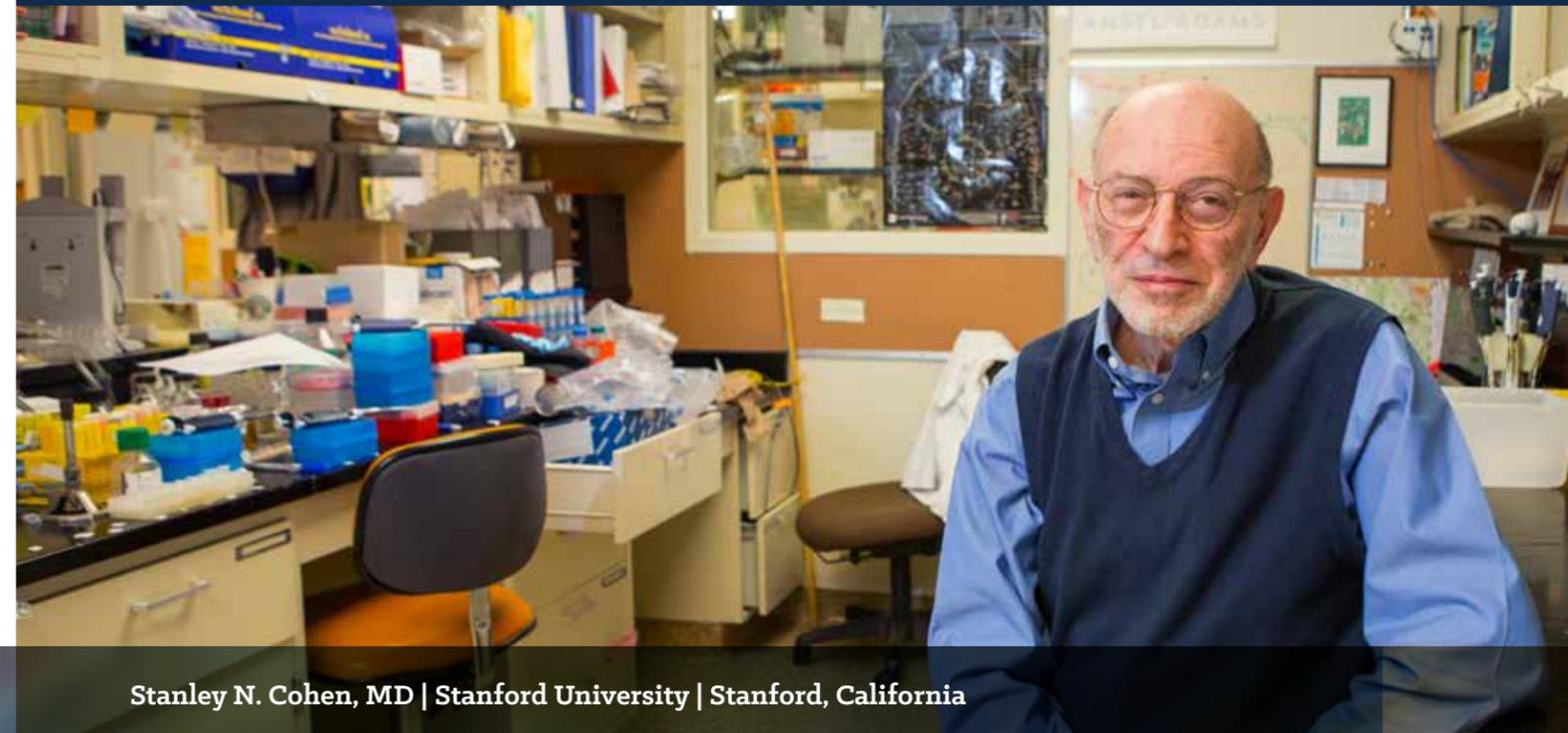
He already has defined a protein agent that blocks the destructive process of local cells in the joints. With assistance from Harrington Discovery Institute experts, Dr. Bottini anticipates moving the protein through preclinical development to ensure its safety and determine how long it persists in the bloodstream.

The critical stage for his project was a laboratory experiment that proved the protein's effectiveness. Dr. Bottini and the other scientists in his lab were anxious as they waited for the results that week, he remembers.

"Most of the time, we are wrong," he says. "We work for that two percent of the time that we get exciting data." He adds, "That is the payoff for being curious."

An INSPIRED RIFF on Research

There's another dimension to Stanley Cohen, MD – Kwoh-Ting Li Professor, Stanford University School of Medicine; renowned geneticist; molecular biologist; Lasker Award recipient; and Harrington Scholar-Innovator – beyond his academic and scientific achievements.



Stanley N. Cohen, MD | Stanford University | Stanford, California

"I'm an old banjo picker," he reveals. In addition to his talent on the five-string banjo, Dr. Cohen also is a published songwriter and plays the guitar.

But there is a connection between his public and private personas. Dr. Cohen's love for banjo-playing and his interest in the legendary folk song writer Woody Guthrie, who died in 1967 at age 52 from Huntington's disease, inspired his research into Huntington's disease. Conducted in collaboration with Taiwan scientist T.H. Cheng, that research eventually led to Dr. Cohen's selection as a Harrington Scholar.

Dr. Cohen's pursuit of the unknown led him and University of California, San Francisco genetic engineer Herbert W. Boyer, PhD, to develop DNA cloning in 1973. Their experiments fundamentally changed the entire approach to biomedical research and laid the foundation for countless advances in medicine and pharmacology over the past 40 years.

Since then, Dr. Cohen's continued fascination with DNA and its role in diseases like Huntington's disease has yielded the discovery that targeting a single gene can circumvent the genetic defects that underlie a family of neurodegenerative diseases. The defect causes repeats of nucleotides, the building blocks of DNA, to expand in length. Expansion of repeats in the gene leads to production of abnormal proteins that cause brain cells to degenerate.

"That discovery led to the notion that if we could target the mechanism that enables expression of expanded repeats, we could benefit patients with the disease," Dr. Cohen explains. "We believe we have the opportunity to treat a collection of neurodegenerative diseases, including Huntington's, each of which is monogenetic – caused by a defect in a single gene."

Even after more than five decades of biomedical research, Dr. Cohen finds the possibility of launching a successful treatment for Huntington's exciting. "I would like to see this happen while I am here to enjoy it."

A humble man and a scientist to his core, Dr. Cohen expresses his thoughts about his legacy to medicine. "I love the process of discovery," Dr. Cohen says. "I'm excited by research. I don't want to be remembered for one thing but as someone who asked important scientific questions during his career."

"I love the process of discovery. I'm excited by research. I don't want to be remembered for one thing but as someone who asked important scientific questions..."

Just BREATHE



Benjamin M. Gaston, MD | Case Western Reserve University | Cleveland, Ohio

The rapid gasping and grunting of a young child having breathing difficulties are distressing to witness and hard to forget.

Harrington Scholar Benjamin Gaston, MD, is Director of the Pulmonary Research Institute at Case Western Reserve University School of Medicine and Chief of the Pulmonary Division at University Hospitals Rainbow Babies & Children's Hospital. In his early years as a pediatrician in the 1980s, Dr. Gaston encountered dozens of children in respiratory distress. Those memories have stayed with him.

"The most difficult patients I saw in those days were those who had respiratory disease," he recalls. "At the time, our options were really limited. It was hard to make them better and to keep them healthy."

This critical need drove him to undertake a research fellowship to study pediatric breathing problems at Boston Children's Hospital. "I wanted to help solve those problems. I'm thankful to be involved in research that has created more options for these children," Dr. Gaston explains. That experience helped set the course for his career in pediatric pulmonology.

As a physician-scientist, he has translated basic science into a potential treatment for cystic fibrosis and developed potential treatments for children with the most severe forms of asthma.

Now, with support from Harrington Discovery Institute, Dr. Gaston is developing a first-in-class drug to stimulate the drive to breathe. This type of therapy is critically needed in treating infants and children and also in older patients, in settings ranging from the ICU to the battlefield.

Dr. Gaston is hopeful that this drug will decrease the risk of respiratory side effects from the use of pain medication in children. "We want to help resolve a chronic disconnect faced in all children's hospitals: We hope the drug will enable children to breathe normally while, at the same time, having adequate sedation and pain control," he explains.

Central to Dr. Gaston's approach to patient care today is the same desire to solve his young patients' problems that motivated him 30 years ago. "I try to think through innovative options to help each child," he explains. "I always try to stay optimistic about what we can do to improve a child's outcome."

HARRINGTON DISCOVERY INSTITUTE:

Dr. Gaston, why did you choose pediatrics as your specialty?

DR. GASTON: *I knew it would be fun and rewarding to come to work. When the pediatrician can solve the puzzle of a child's disorder, the child often gets dramatically better. I'm thankful that Harrington Discovery Institute provides new resources to solve some of the more difficult puzzles.*

Serendipity, Rejection and THE FUTURE

It's been more than half a century since James Hardy, MD, performed the first human lung transplant on a 58-year-old man in Jackson, Mississippi, and today doctors worldwide perform more than 2,000 lung transplants each year. Even with surgical advances, rigorous selection of patients and donors, and modern medical care, the average patient survives just five and a half years after transplant.

"Unlike other solid organ transplantation, half of lung transplant patients have chronic rejection," notes Rama Mallampalli, MD, Division Chief of Pulmonary, Allergy and Critical Care Medicine at the University of Pittsburgh.

Intrigued by pulmonology since his fellowship at the University of Iowa, Dr. Mallampalli has a burning desire to develop an antirejection medicine more effective than prednisone and without the side effects. As a pulmonary consultant at the University of Pittsburgh Medical Center, his interactions with patients in intensive care are a potent reminder of the need for a new, better treatment, and these interactions invigorate his research.

Dr. Mallampalli set his future path while he was Professor of Medicine and Biochemistry and Associate Chair of Pulmonology at Iowa. In his lab, he serendipitously discovered a new protein that stimulates the immune system to cause inflammation. He hypothesized that the protein is involved in switching on a process that initiates transplant rejection.

Two years after moving to Pittsburgh in 2009, Dr. Mallampalli and his research team, including University of Pittsburgh Medical Center transplant pulmonologist John McDyer, MD, proved that giving a compound that blocks the protein's activity prevents transplant rejection. In 2012 he filed a patent. As a Harrington Scholar, he anticipates further testing in the lab to move the compound closer to the clinic.

"It always begins with patients for me," Dr. Mallampalli stresses. "This is an opportunity to bring forth a brand-new strategy to help patients." He believes his drug may be the first member of a new family of antirejection, anti-inflammatory drugs.

Dedicated as he is to both his patients and his research, Dr. Mallampalli is passionate about encouraging the next generation of physician-scientists. "The physician-scientist has a unique opportunity to make an indelible mark in discovering new treatments and translating research from the lab to the patient," he says.

"Today's clinical fellows, trainees in research programs, medical students – they are the next generation who will find the new cures."



Rama K. Mallampalli, MD | University of Pittsburgh | Pittsburgh, Pennsylvania

PSORIASIS FAST FACTS

How many people have psoriasis?

2 to 3 percent of people

How is psoriasis treated?

Psoriasis typically is treated with drugs given orally or by injection that suppress the immune system

Why is a new treatment needed?

Lifelong immunosuppression can cause many side effects, from headaches to kidney and liver damage

Putting Some Skin in the GAME

M. Peter Marinkovich, MD, Associate Professor of Dermatology at Stanford, characterizes himself as “a lab rat at heart who also loves seeing patients.” His Harrington Discovery Institute project, a potential cure for psoriasis, happily gives him time for both.

Dr. Marinkovich traces his interest in dermatology back to his three-year stint as an Army medic in the late 1970s when he treated dozens of soldiers with burns, wounds and other skin injuries. When he returned to college after the Army to complete his degree, he had the opportunity to pursue skin-related research. By the time he entered St. Louis University School of Medicine, “I had a pretty good idea I would like to do dermatology as a specialty,” he says.

With dermatology’s usually predictable office hours, it offered the added attraction of ample research time. For Dr. Marinkovich, dermatology has been the ideal combination of clinical practice and basic research. For many years his focus in both was epidermolysis bullosa, a genetic blistering disease. In fact, Dr. Marinkovich is credited with discovering the disease’s molecular basis.

The root cause of epidermolysis bullosa is a defect in a gene that encodes a protein in the skin. Through a series of biologic pathways, the mutation leads to blistering. As Dr. Marinkovich’s research progressed, he determined that this same protein’s activity also underlies psoriasis.

“When we proved that superactivating this protein caused psoriasis in mice, that’s when we knew we had something,” Dr. Marinkovich says, recalling his personal “Aha!” moment. “After that, I got fully involved in psoriasis research, and I started seeing psoriasis patients in clinic.”

Fueled by the excitement of their initial discovery, Dr. Marinkovich and his research team tested dozens of existing drugs to find one that could inhibit this protein at the molecular level. In 2014, they found that the diuretic benzamil caused “significant reversal” when given as an injection or cream.

Dr. Marinkovich anticipates that with Harrington Discovery Institute’s support, he will prove benzamil’s effectiveness in human skin cells.

Ultimately, this potential new product may satisfy Dr. Marinkovich’s deepest desire. “When I retire and look back at my career, I want to feel like I made a difference,” he explains. “I think this project is giving me the opportunity to do that.”

That would make an impressive legacy for a “lab rat.”



M. Peter Marinkovich, MD | Stanford University | Stanford, California

A HEART for Children

David Milan, MD, has a heart for children with long QT syndrome, a rare, congenital disorder. A type of abnormal heart rhythm, a long QT interval causes a fast, irregular heartbeat, fainting and an increased risk for sudden cardiac death.

“We can treat older patients with a defibrillator,” Dr. Milan explains. “But for kids, a defibrillator is a big deal. They will require multiple surgeries and multiple lead replacements during their lifetime.” Treatment with beta blocker drugs can be effective, but comes with significant side effects, especially for children.

A cardiologist and Assistant Professor of Medicine at Harvard Medical School, Dr. Milan says he always found heart rhythm disorders the most fascinating subspecialty in his field. He notes that numerous medical advances in diagnosing and treating heart rhythm disorders have been made in the past 10 years, but not for long QT syndrome.

As a researcher, Dr. Milan feels driven to find a treatment for these young patients. “That combination of research and patient care is what motivates me,” he stresses. “Seeing patients every day gives us an added kick in the pants to find a treatment and keeps us focused on translational research.”

Now, after years of studying long QT syndrome clinically and in the lab, he believes he may have a solution. The key may be a compound that prevents prolonged QT syndrome upstream from its origin.

Dr. Milan and his team have identified a compound that first successfully blocked long QT syndrome in zebrafish and then in human stem cells in a test tube. The pivot point, Dr. Milan recalls, was when his ever-skeptical post-doc

fellow came to him and reported that the compound not only stopped the arrhythmia in rabbits, but he was unable to create an arrhythmia in animals treated with the compound.

A California native, Dr. Milan graduated from Stanford with a degree in chemistry and started his career as a pharmaceutical company chemist. In that role, he realized that the connection with patients was remote. “I wanted to interact with patients and see the fruits of my labor. That’s what drove me to medical school,” he recalls.

Dr. Milan looks to 2014 Harrington Prize winner Hal Dietz, MD, as his personal role model. “He is an inspirational figure for me,” Dr. Milan says. “He is very focused on drawing that connection between patients and research. Our roots are in basic discovery, but for me there is always a compelling need to help patients.”



David J. Milan, MD | Massachusetts General Hospital | Boston, Massachusetts



Kevin D. Niswender, MD, PhD | Vanderbilt University | Nashville, Tennessee

Tapping Into the COLLECTIVE GENIUS

Kevin Niswender, MD, PhD, Associate Professor, Medicine and Molecular Physiology and Biophysics at Vanderbilt University School of Medicine, steadfastly follows two principles in his professional life: develop those around him and tap into the collective genius.

Both are apparent in how he approaches his research. Dr. Niswender has a passion for research in the team setting with a connection to patient care. “When I learn what struggles my patients are experiencing, it feeds back to my research,” he says.

Trained as a physician-scientist with a PhD in glucose metabolism, Dr. Niswender has studied the neural control of metabolism for 15 years. Now, he and his team are tackling a therapeutic approach that they believe will address diabetes, obesity, and comorbid neurologic disorders such as depression and Alzheimer’s disease. They are developing small molecules that modulate glucagon-like peptide-1 receptors found throughout the brain.

In his clinical practice, Dr. Niswender treats patients with obesity, metabolic syndrome and poorly controlled diabetes who often are depressed and struggle with motivation and cognitive control. “We’re excited that targeting this receptor in this way may improve both the metabolic and neurologic aspects of disease,” he says.

His experience includes involvement in clinical trials as well as basic science. With his current project, he says, he is excited to be in “this translational phase of the drug development process” with Harrington Discovery Institute.

“I know this is an uphill battle and the likelihood of success is low,” he admits. “But Harrington Discovery Institute has tremendous expertise to help us move ahead.”

Although Dr. Niswender and his team believe their approach will be effective for multiple diseases, for the immediate future they will focus on diabetes, he says. Of all the possible directions they could take, the path for drug development to treat diabetes “is the most straightforward,” Dr. Niswender notes.

This project holds the potential for generating attention from the public, the media and the medical world, but Dr. Niswender doesn’t relish the spotlight. His family helps keep him grounded, he says. Despite his busy research and clinical schedule, he makes time for cooking with his wife and children, coaching his daughter’s sixth-grade basketball team and simply spending time with his family.

Not surprisingly, Dr. Niswender’s greatest satisfactions in his professional life are not related to fame. “I find it very rewarding to understand the physiology [of the disease process] through research and apply it to patients in the clinic, and to take what my patients teach me about their struggles back to the lab,” he says. “I also get great satisfaction teaching and mentoring young physician-scientists.”

From BENCH TO BEDSIDE to Defeat Sickle Cell Disease

A summer job for Susan Perrine, MD, ignited her lifelong interest in sickle cell disease and beta thalassemia, two related, genetic blood diseases.

"I was working in Saudi Arabia on a public health project on trachoma, an infectious, blinding eye disease that affected many infants there," she remembers. "I also learned that sickle cell disease also was prevalent in the oasis region. Normally it is a serious blood condition, but the patients were not sick because they had adapted by producing large amounts of fetal hemoglobin."

High levels of fetal hemoglobin – the oxygen-carrying component of blood in infants before birth – are known to protect against many problems in sickle cell disease and beta thalassemia. Usually by the time a baby reaches 6 to 12 months of age, fetal hemoglobin production declines significantly, and adult hemoglobin replaces most of the prenatal form.

"American physicians caring for families in the region were collaborating with Oxford scientists on the mystery of how fetal hemoglobin persisted in the population," Dr. Perrine continues. "I was charged with carrying blood to London for studies on what seemed an important mission."

Her experience in Saudi Arabia led her ultimately to pursue a fellowship in pediatric hematology-oncology at Boston's Dana-Farber Cancer Institute. As a fellow, she treated

many children who were very sick with sickle cell disease or beta thalassemia. "It bothered me that the fetal hemoglobin gene (that produces the hemoglobin protein) turns off on a fixed developmental timetable, allowing mutant genes to turn on and cause disease," she says.

Years later, the innate remedy for these two blood diseases still inspires her search for a therapeutic to reproduce "nature's cure." Now a hematologist-oncologist at Boston University School of Medicine, she is close to developing a medication to restore fetal hemoglobin production. But advancing the latest therapeutic to the clinic has been fraught with challenges.

"I have traveled between the bench and the bedside a couple of times," Dr. Perrine says. Two compounds appeared promising in the laboratory, but the first required intravenous injection and the second had more favorable properties, but was less active in some patients.

Back at the bench, she discovered a higher-potency oral drug that is approved for another condition, with a benign safety profile. But, the U.S. Food and Drug Administration is requiring many additional tests because test standards expanded since this drug was first approved.

"I want to develop this," Dr. Perrine says with determination. "I want to get something to patients that will truly make a difference."

She has completed some required testing, but came to a halt due to lack of funding. At this point, Dr. Perrine admits she feels thwarted. "Having to stop is very frustrating," she says. "We know how to streamline clinical trials in these diseases. With funding, this drug could be in patient trials within a year."

She is looking to Harrington Discovery Institute to help complete the FDA-required testing to initiate clinical trials. She already can visualize the difference treatment can make for patients.

"Patients' health is continuously deteriorating in these diseases," she says. "To treat them by reactivating this innate gene would make the difference between really helping to prevent the damage compared to relieving pain, but not stopping the damage."



Susan P. Perrine, MD | Boston University | Boston, Massachusetts

WHAT IS SICKLE CELL DISEASE?

Sickle cell disease is a group of inherited disorders in which abnormal, sickle-shaped red blood cells are produced. Hemoglobin is the blood protein that delivers oxygen to all the cells, tissues and organs in the body. Misshaped sickle cells adhere abnormally to blood vessels, causing inflammation, tissue ischemia, organ damage, strokes and other serious problems. Children with sickle cell disease start to experience painful symptoms and develop anemia when they naturally transition from fetal to the adult form of hemoglobin.

Scientists have known for decades that high levels of fetal hemoglobin inhibit the formation of sickle-shaped red blood cells in babies born with sickle cell genes and alleviate anemia in both blood diseases. Newborn and young infants produce high levels of fetal hemoglobin, the form that is made while the baby is in the womb. When this form turns off, children develop the diseases, including hemolytic anemia and cardiac stress in children with thalassemia.

For at least 40 years, scientists have studied molecular mechanisms to reactivate fetal hemoglobin production to benefit patients with these diseases. The means to accomplish it appear clear, lacking only the funding to put small molecule therapeutics into practice.

Ann Marie Schmidt, MD | NYU School of Medicine | New York, New York



In Pursuit of the REAL BOTTOM LINE

In speaking with Ann Marie Schmidt, MD, or reviewing her extensive list of medical research accomplishments and accolades, it's difficult to imagine that she ever lacked self-confidence or endured bullying in school. "It was difficult being the girl who loved science, but the bullying didn't bother me enough to deter me from my goals," she recalls. "Fortunately, even then I had an inner strength."

She set her goal of medical school early in life, an unusual career choice for a girl in the 1970s and one sure to attract negative attention from her fellow students. Dr. Schmidt credits her high school biology and chemistry teachers for supporting her dream. "They recognized my ability in science and pushed me to excel," she explains.

Even so, she still lacked complete confidence in herself and applied to New York University School of Medicine (NYU) through the school's early decision option, "to give myself that extra chance for success," Dr. Schmidt says. She was accepted in the spring of her junior year in college. Finally confident of achieving her goal, she enrolled at NYU School of Medicine, fully intending to become a clinician.

Her goal shifted slightly as she went through her post-graduate training. "I realized that what I was missing was an understanding of how the biology worked," Dr. Schmidt recalls. "Then I did a research fellowship, and that was my point of no return." She credits Robert Silber, MD, her NYU fellowship director at the time, with persuading her to take a serious interest in laboratory research.

Dr. Schmidt, now Professor of Medicine, Pharmacology and Pathology at NYU, studies inflammation with the same focused determination she pursued in medical school. She and her team

have identified RAGE, a receptor on the cell surface that increases inflammation in seemingly disparate disease such as diabetes, rheumatoid arthritis and Alzheimer's disease.

They are searching for a small molecule modifier that can potentially alter the RAGE pathway to reduce inflammation. Working with Harrington Discovery Institute, their first disease target will be diabetes with the intent of eventually expanding their scope to inflammatory changes in brain blood vessels and immune cells that are associated with Alzheimer's disease.

The work is intensely challenging, Dr. Schmidt notes, particularly being able to translate laboratory research to a treatment. Despite difficulties and setbacks – including losing all of her experimental mice and most of the laboratory's stored samples in Superstorm Sandy – she continues for two personal reasons.

"The bottom line is the realization of how terribly awful these diseases are," she says. "And secondly, this is how I can give back to the community and those who have supported me in my journey."

War and Peace and DIABETES

A promising treatment for type 2 diabetes (T2D) and nonalcoholic fatty liver disease (NAFLD) in development by Gerald I. Shulman, MD, PhD, and his colleagues at the Yale Diabetes Research Center has its unlikely origins in French munitions factories a century ago.

At the turn of the 20th century, it was noted that French munition workers ended each workday covered with dust used in the manufacturing process. They felt fatigued, sweated excessively, had elevated body temperature and lost weight. Researchers discovered that the dinitrophenol (DNP) in the dust was responsible for these symptoms.

Based on these observations, DNP was then used in humans without prior safety and efficacy studies and, in the 1930s, hundreds of thousands of individuals were taking DNP, which was available as an over-the-counter medication for weight loss. But in 1938, the U.S. Food and Drug Administration banned the compound, based on several reports of hyperthermia leading to death.

Dr. Shulman, who is the George R. Cowgill Professor of Medicine and Cellular & Molecular Physiology and an Investigator of the Howard Hughes Medical Institute, is taking another look at DNP, this time as a potential treatment for T2D and NAFLD. "Insulin resistance is the primary factor that drives the development of T2D, and we had previously established that ectopic lipid in liver is the primary cause of insulin resistance. To test this hypothesis, we showed that low-dose DNP treatment

reduced liver fat content and reversed liver insulin resistance in rodent models of NAFLD. The key thing is whether we could improve the therapeutic window of DNP and dissociate the hyperthermia from the lipid-lowering effect to make this a viable drug target."

Through pharmacokinetic studies, he found that the toxicity of DNP was related to the peak plasma concentrations whereas all that was required to reverse liver fat and insulin resistance were DNP concentrations that were more than a hundred-fold lower. He went on to develop a controlled release formulation of DNP, called CRMP, which he showed reversed hyperlipidemia, insulin resistance, T2D, inflammation and liver fibrosis in rodent models of T2D and nonalcoholic steatohepatitis (NASH) with a five-hundred-fold increase in the therapeutic window.

With Harrington Discovery Institute support, Dr. Shulman will pursue IND (investigational new drug) enabling studies of CRMP as well as develop other liver-targeted mitochondrial protonophores.

What a difference a century makes in medical science.



Gerald I. Shulman, MD, PhD | Yale University | New Haven, Connecticut

THE MAKING OF A DIABETES SPECIALIST

Some of Dr. Shulman's earliest memories are those of childhood summers at a camp for diabetic children in Michigan where his father was the staff diabetologist. Nonetheless, Dr. Shulman senior thought radiology would be the ideal fit for his son, one that combined young Gerald's love of physics with medicine.

In medical school, though, Dr. Shulman gravitated toward endocrinology and metabolism. "I loved biochemistry and physiology," he recalls, "and the endocrinologists that taught me were some of the best scientists and physicians that I knew – they were able to readily combine basic science with clinical medicine to improve patient care, which was what I wanted to do."

Oxford-Harrington Scholar Programme

Harrington Discovery Institute, in November 2014, formed an affiliation with the University of Oxford in the United Kingdom to create the Oxford-Harrington Scholarship Programme. Each year up to three scholars are selected.

Oxford-Harrington Scholars are physician-scientists from the University of Oxford who are working to translate discovery science into medicines that improve human health. Scholars receive strategic advising and mentoring from experts in pharmaceutical development through Harrington Discovery Institute's Innovation Support Center to chart a path from the bench to the clinic.

Helen McShane, MD, PhD, FRCP
University of Oxford
Oxford, UK



Developing a Life-Altering Vaccine

Five thousand miles separate Dr. Helen McShane's laboratory at the University of Oxford in the UK and the small African villages and cities where she hopes to make an impact on children's health.

A specialist in infectious disease, Dr. McShane, a Professor of Vaccinology at the University of Oxford, has devoted more than 15 years to developing a vaccine for tuberculosis (TB).

BCG, the only available vaccine against TB, was developed in 1908. Administered at birth, it protects children against severe disease and TB meningitis until age 10 but offers no immunity against lung disease, the form of TB that accounts for most of the TB-related illness and death worldwide. "We know that boosting with BCG (giving it repeated times) doesn't make any difference and doesn't make it any better," Dr. McShane adds.

Since 2002, Dr. McShane's research team has conducted more than 20 clinical trials of new TB vaccines in the UK, The Gambia, Uganda, Senegal and South Africa. In 2013, they completed an efficacy trial of the most-promising vaccine, MVA85A, given as a booster after BCG. In the first efficacy trial of a new TB vaccine since 1968, researchers administered the MVA85A to nearly 2,800 infants in South Africa.

The results made headlines around the world: MVA85A was not any more effective at protecting infants from TB than BCG alone. "It was disappointing because it made clear that we do not know the immunology – why the vaccine didn't work," Dr. McShane notes.

As a researcher, Dr. McShane's reaction has been fascination rather than frustration and an intensified motivation to find the answers. "You do a clinical trial and get results and evaluate why it did or didn't work," she explains. "It's a fascinating process and it shapes the next steps."

Dr. McShane traces her career-long absorption with infectious disease to her residency at a hospital in Brighton, UK, where she cared for HIV patients in the 1980s. At that time, patients were very ill and died soon after admission. This grim experience led to a career-changing decision for Dr. McShane – to combine clinical care with infectious disease research. With the field of HIV research already crowded, she selected TB, a "more interesting bug," as her concentration.

Fifteen years later, Dr. McShane continues to be inspired by the combination of clinical work and research. "I like the balance of the immediate gratification in treating patients and the long-term gratification of research."

Her unflagging pursuit of a better TB vaccine coupled with the expertise of Harrington Discovery Institute's Innovation Support Center hold the promise of both kinds of rewards.

Claudia Monaco, MD, PhD, FESC
University of Oxford
Oxford, UK

20 YEARS IN THE MAKING: A New Approach to Heart Disease

Ask Oxford-Harrington Scholar Claudia Monaco, MD, PhD, FESC, how she achieves work-life balance while juggling her marriage to a fellow scientist, the demands of their two-year old son and her physician-scientist career, and she laughs. “I don’t even know what that is,” she responds. Dedicated to her family, her research and her patients, she describes her life as “complicated and rewarding.”

Born in Italy and educated in Rome, Dr. Monaco credits an old-time physician and his wooden stethoscope who treated her during her childhood as her inspiration for becoming a doctor. Although she pursued classical studies in college, her love for medicine and intellectual curiosity won out, and she enrolled in medical school instead of pursuing a career as a classics scholar.

Her captivation with atherosclerosis began in Rome during her fellowship training in cardiology under the tutelage of Attilio Maseri, PhD. “He inspired me to be inquisitive about the disease and not just accept current thinking,” Dr. Monaco says. She participated in the first studies of the systemic inflammatory response triggered by the immune system in patients with certain types of heart disease.

In 1998, Dr. Monaco left behind her native country’s sunshine and renowned cuisine for the opportunity to pursue intensive atherosclerosis research in London. The relocation posed some daunting personal challenges, but Dr. Monaco was eager to join the Kennedy Institute of Rheumatology. “There were no equivalent positions in Rome,” she explains. “I wanted the intellectual freedom to pursue my own projects.”

In London, she found a mentor in Marc Feldman, PhD, whom she credits with directing her toward translational research. “He would ask what you surmise from your data that could be therapeutic,” Dr. Monaco recalls. “He directed my curiosity in the right direction.”

She recently has relocated again, moving with the Kennedy Institute from London to Oxford where she is Professor of Cardiovascular Inflammation. Her long quest to translate her research into patient care finally is coming to fruition. Dr. Monaco and her team have shown that certain immune receptors increase inflammation in atherosclerosis, causing blood vessel damage, while others are protective.

“We believe there is a repair pathway for the blood vessels that we could selectively activate,” she explains. With assistance from Harrington Discovery Institute experts, she has identified a small molecule that can be modified to target that pathway.

Although foregoing clinical practice would free up more time to advance her research, Dr. Monaco is reluctant to give up her patients. “There is something about treating patients and seeing them get better that is rewarding,” she notes.

Research offers a different type of fulfillment, Dr. Monaco shares. “Sometimes you have a eureka moment when you discover something new, and you are the only one who knows about it,” she explains. “Once you experience that feeling, you cannot wait until your next discovery to feel it again.”



Alzheimer's Drug Discovery Foundation-Harrington Program

Harrington Discovery Institute and its foundation partner Alzheimer's Drug Discovery Foundation (ADDF) share a common mission in the fight against Alzheimer's disease: accelerating scientists' efforts to develop drugs to prevent, treat and cure Alzheimer's disease, related dementias and cognitive aging.

The mission-aligned partnership leverages the combined expertise and resources of the two organizations to advance highly promising Alzheimer's disease discovery projects conducted in academic medical institutions nationwide. Created in 2013, the ADDF-Harrington Scholar program supports up to three physician-scientists per year.

ADDF-Harrington Scholars receive funding from ADDF and strategic advising and mentoring from experts in pharmaceutical development through Harrington Discovery Institute's Innovation Support Center to accelerate their discoveries toward clinical impact.

Carol A. Colton, PhD
Duke University
Durham, North Carolina



Blazing a New Trail for Alzheimer's Patients

Carol Colton, PhD, receives dozens of emails and letters, burdened with tears, saturated with hope for a cure, for better treatments, for a lifeline of any kind. They come from family members of people with Alzheimer's disease, reaching out to Dr. Colton for some glimmer of light in the darkness of this terrible disease.

They have heard that Dr. Colton, Professor of Neurology at Duke University School of Medicine, is blazing a new path in Alzheimer's disease research, a path that may lead to an innovative treatment approach. Dr. Colton's research focuses on the body's immune response to Alzheimer's disease. "Evidence supports the idea that the immune system, which protects our bodies from foreign invaders, plays a part in contributing to the disease," Dr. Colton explains.

Microglia, a type of immune cell that moves rapidly to the site of injury in the brain to help it provide, repair and survive, are the first responders to infection. Research conducted at Duke shows that microglia begin to divide and change early in Alzheimer's disease. Instead of fighting off invaders and protecting the brain, the immune mechanism somehow goes haywire in the brain.

Dr. Colton and her research team determined that microglia in Alzheimer's disease chew up an important amino acid, arginine. Arginine deprivation appears to be related to Alzheimer's disease. "When we blocked this process with a small-molecule drug, we prevented memory loss and structural changes in the brain in laboratory mice that carried familial Alzheimer's," Dr. Colton explains.

The laboratory trial that yielded such dramatic results was complex and lengthy, but set the course for her future research, she says. Her ultimate goal is to block the process at the onset point and prevent Alzheimer's in susceptible patients or prevent its progression in patients with early-stage disease. With Harrington Discovery Institute's assistance, her drug is moving rapidly toward the possibility of a clinical trial, more quickly, she says, than she would have believed possible.

Neurodegenerative diseases like Alzheimer's are very complex, she notes. "I feel like I have been doing a giant puzzle, and I keep trying to fit the pieces together." In the face of that complex puzzle, the emails and letters from families will not allow her to get discouraged or give up, she adds.

"The emotional and physical suffering from Alzheimer's is immense, and people are terrified of it," Dr. Colton says. "I truly believe we can successfully fight this disease."

From Skeptic to Believer

The brain has been called science's last frontier. The very epicenter of what distinguishes humans from other life forms, the brain remains largely uncharted territory. The potential mysteries yet to be solved are what attracted Jerri Rook, PhD, Assistant Professor of Pharmacology at Vanderbilt University, to neuroscience research.

Since 2011, she has been focused on the brain chemistry of Alzheimer's disease, a field where there are still more questions than answers. "There is a huge unmet need for treatments. Alzheimer's will be an increasing burden as society ages, complicated by the fact that these days families don't live as close to each other," Dr. Rook says.

The cause of Alzheimer's remains unknown, she adds, although we are learning more about the brain circuitry that affects cognition. One chemical in the brain in particular, acetylcholine (ACh), is known to be closely linked with memory deficits. It appears that in Alzheimer's disease, lesser amounts of ACh are available in the brain. Dr. Rook's therapeutic approach is to increase the activity of a specific target of ACh in the brain, the muscarinic acetylcholine receptor subtype 1 (M1), to reverse the cognitive symptoms related to Alzheimer's disease.

Dr. Rook and her research team have identified a candidate drug that is highly selective in increasing this activity. She is enthusiastic about the potential it may hold for treating Alzheimer's disease by ameliorating the heartbreaking dementia associated with this progressive neurodegenerative disorder.

"Initially we couldn't help but be skeptical," she says. "These compounds have been pursued by many others unsuccessfully. But now we are very excited because we continue to find more and more consistent results."

Dr. Rook and her team are not the first or the only researchers to be targeting ACh transmission as a therapeutic approach. She anticipates encountering serious competition in the race to market, including a similar drug already in clinical trials. Dr. Rook says she is looking to Harrington Discovery Institute and the Innovation Support Center's "unprecedented degree of expertise" to help her successfully cross the Valley of Death.

She stays positive and motivated by looking to the future, one without the devastation wrought by Alzheimer's disease. "What would be most rewarding would be to get a new drug into the clinic that actually makes a difference," she comments.

With the intensive research and responsibility her daily work entails, Dr. Rook seeks peace and relaxation in the outdoors whenever she can. An avid outdoorswoman, she tries to leave the lab behind occasionally and re-energize by playing volleyball, kayaking and hiking the lush countryside around Nashville.

Jerri M. Rook, PhD
Vanderbilt University
Nashville, Tennessee



"It's not just the hope that this new medicine will help Brian, but the idea that every medication he can take, other people with Alzheimer's at one point were willing to test. That's why we did it."

Fran FitzSimons, patient story begins on page 40

A Family's BRAVE CHOICE

Brian and Fran FitzSimons were enjoying life since Mr. FitzSimons retired at the end of 2012. Their home near Lake Erie in Euclid, Ohio, served as home base in between their travels and visits to their out-of-town daughters and their grandchildren. In their mid-60s, the FitzSimons had mapped out their plans for many happy years ahead.

Their retirement plans shifted course in 2014, beginning with a simple stop for gas. Mr. FitzSimons pulled out a credit card to pay for his purchase and stood there, looking at the card, not knowing what to do. "That triggered memories of my mother who years before had similar complaints. Looking back, I think I diagnosed myself," he recalls.

Alan Lerner, MD, Director of the University Hospitals Neurological Institute Brain Health & Memory Center at UH Case Medical Center, confirmed what Mr. and Mrs. FitzSimons suspected. Mr. FitzSimons was in the early stages of Alzheimer's disease.

Since the diagnosis, Mr. and Mrs. FitzSimons have come to appreciate firsthand the significance of research into potential new treatments that may slow or even reverse the disease. When Dr. Lerner presented the couple with the option of participating in a clinical trial of a new medication, one of more than 70 Alzheimer's trials underway at UH, "I decided right away to do it," Mr. FitzSimons says.

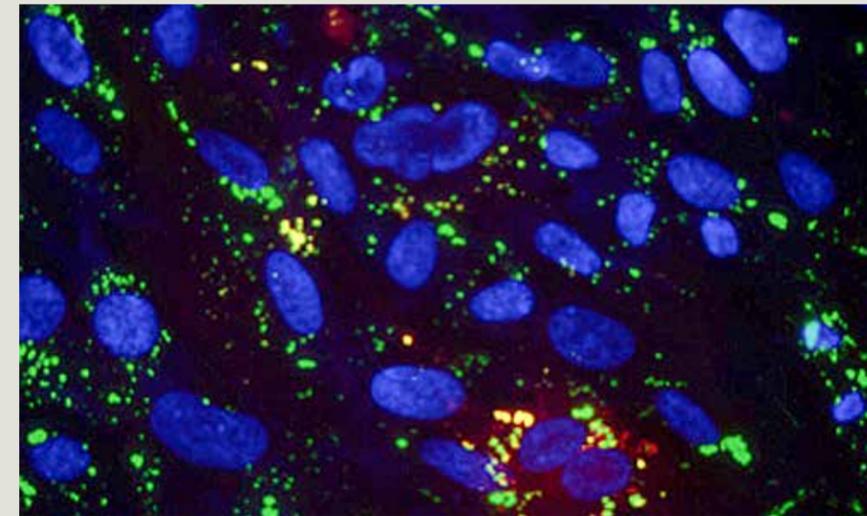
"There are a lot of new treatments being worked on," he adds. "I want to do whatever I can to be helpful to others."

Mrs. FitzSimons chimes in, "It's not just the hope that this new medicine will help Brian, but the idea that every medication he can take, other people with Alzheimer's at one point were willing to test. That's why we did it."

Mr. FitzSimons' current medication trial ends in November 2016. He is optimistic there will be another one in which he can participate. At this point, Mrs. FitzSimons says, their best hope is that her husband's condition, with the help of the latest drugs, will plateau.

For now, she says, "We do anything we can, and we are having fun." The couple travels as much as possible and spends time with their family, particularly one of their daughters who relocated back to the Cleveland area from Boston. Another daughter has taken sabbatical from her university job in Madison, Wisconsin, to be with her father. A third daughter lives in India but stays in close contact with her family.

"We all are staying positive. There is so much research to try," Mrs. FitzSimons says. "Hope, that's what we have."



WHAT ARE MISFOLDED PROTEINS AND WHY ARE THEY IMPORTANT FOR HUMAN DISEASE?

On the surface, disparate diseases such as Alzheimer's and diabetes seem unrelated. Researchers now know that these diseases and a long list of others share a common cause – proteins that are misfolded.

At the cellular level, proteins participate in virtually every biologic process in our bodies. When a protein is flawed, it is easy to see that it could cause a process to go awry. Our DNA contains the recipes or genetic codes for constructing proteins. Genetic mutations change the recipe and can result in an unstable protein.

Normal proteins fold in a certain way that makes them soluble and allows them to function correctly. Unstable proteins misfold and are either useless or toxic. They are insoluble and tend to clump in formations called amyloids or aggregates. Sometimes the toxic protein can interact with normal proteins and change them into toxic forms. In addition to genetic mutations, exposure to environmental toxins, structural changes to a protein, or chance also can cause misfolds.

When amyloids develop in the central nervous system, they can cause Parkinson's, Alzheimer's or other neurodegenerative diseases. Development of amyloids in tissues outside of the central nervous system can cause a wide array of diseases, including diabetes, heart disease, liver disease and cataracts.

Harrington Scholar-Innovators are developing treatments for a number of diseases based on eliminating toxic misfolded proteins or correcting the genetic mutation that results in protein misfolds.

Gund-Harrington Scholar Program

In 2014, the Foundation Fighting Blindness became the second disease-focused foundation to partner with Harrington Discovery Institute. As a result of the shared commitment to accelerate cures for retinitis pigmentosa and other retinal diseases, the National Center for Excellence in Fighting Blindness, a Gund-Harrington Initiative was formed. Through this initiative up to three Gund-Harrington Scholar awards are made each year.

Gund-Harrington Scholars are innovative scientists and physicians selected from the U.S. and Canada whose research has the potential to advance medical therapies for those suffering from inherited retinal degenerative diseases. In addition to funding, scholars also receive strategic advising and mentoring from experts in pharmaceutical development through Harrington Discovery Institute's Innovation Support Center to advance their discoveries to the clinic.



Albert R. La Spada, MD, PhD
University of California, San Diego
San Diego, California

A Vision for the Future

Call it beginner's luck, a eureka moment or scientific intuition.

Albert La Spada, MD, PhD, now Professor and Division Head of Genetics in the Departments of Pediatrics and Cellular & Molecular Medicine at the University of California, San Diego, was a 26-year-old graduate student in the MD-PhD program at the University of Pennsylvania School of Medicine in 1991 when he made his first contribution as a physician-scientist.

Dr. La Spada discovered a previously unknown type of genetic mutation that identified the cause of a rare neurologic disease called Kennedy's disease. With the resulting paper published in *Nature*, the leading science research journal, his discovery heralded the emergence of a new field of study in neurodegenerative diseases.

It was a heady experience for a young physician-scientist. "It was pretty incredible, cool and very exciting," says Dr. La Spada, looking back to the event that took place 25 years ago.

The mutation he discovered does its damage by creating repeated series of amino acids in a gene. By the late 1990s, researchers had determined that this type of mutation, known as an expansion, causes a buildup of proteins in the cell that start to fold incorrectly. Clumps of misfolded proteins are characteristic of all neurodegenerative diseases.

Using the building blocks laid by his own discovery and later refinements to it, Dr. La Spada now is developing a potential treatment for retinal diseases.

The connection was a 1997 discovery by a French group of scientists. They reported an expansion mutation and protein misfolds in SCA7, a nervous system disease that also causes vision problems.

This discovery redirected Dr. La Spada's interest to the biology of the retina and protein misfolding. With the support of Harrington Discovery Institute, he now intends to develop a treatment for retinal diseases and then apply the same science to SCA7 brain disease.

"I love research," says Dr. La Spada, who sees patients with SCA7 in his clinical practice. "But my greatest passion is for helping patients, and the two are inextricably intertwined. Developing this as a successful intervention for patients would be the ultimate accomplishment."

Dr. La Spada finds immense personal satisfaction in his career. "It's fun and rewarding," he adds. "Each day you don't know what you will learn. If I hit the Powerball jackpot, I would still work because I love it."

Read a patient story about SCA7 on page 48.

Konstantin Petrukhin, PhD
Columbia University
New York, New York



THE UNKNOWN ROBBER: STARGARDT DISEASE

Stargardt disease, often called pediatric macular degeneration, is an inherited, vision-threatening disease that affects children and teenagers. The first symptoms, difficulty in reading and in adapting to bright light, typically appear between ages 6 and 20. In school-age children, problems in school often are the first hint of the diagnosis. An estimated 1 in 10,000 people have Stargardt disease.

Stargardt disease is caused by a genetic mutation that causes the body to create a protein that cannot properly handle vitamin A metabolism in the eye's retina. Vitamin A-derived toxic waste products accumulate in the macula, the center part of the retina. Over time, the light-receiving cells in the macula break

down because of this toxicity. A child or teenager affected by the disease slowly loses vision and by the mid-teens or 20s usually will require vision aids.

Vision loss from Stargardt disease cannot be corrected by glasses, contacts or surgery. There currently is no cure for the disease. The Gund-Harrington Scholar program in partnership with Foundation Fighting Blindness supports promising research to develop a cure for Stargardt disease and other inherited retinal diseases. Notably, Gund-Harrington Scholar Konstantin Petrukhin, PhD, is credited for discovering the underlying genetic mutation for Stargardt disease in 1997.

Preserving a Precious Gift

Beloved faces. The colors of the rainbow. A favorite picture book. Children learn about the world and their place in it through all their senses. They delight in color, movement, images. Imagine, if you can, the limitations vision loss would impose on a child's world.

For the thousands of children and teenagers afflicted with Stargardt disease, those limits are reality. Often called pediatric macular degeneration, Stargardt disease causes progressive vision loss in the eye's center. Although a percentage of the 30,000 people in the United States with Stargardt disease don't experience symptoms until later in life, many people with the disease are visually disabled by the time they reach their early 20s. There is no treatment available.

Konstantin Petrukhin, PhD, Associate Professor of Ophthalmology at Columbia University Medical Center, is hopeful of banishing that dismal prognosis. A specialist in ophthalmic genetics and pharmacology, he is dedicated to developing a drug to treat the genetic defect that causes Stargardt disease.

Vision loss in Stargardt disease is due to degeneration of photoreceptor cells in the eye. This deterioration is believed to stem partly from toxicity caused by derivatives of retinol, which is needed for vision, Dr. Petrukhin explains.

Dr. Petrukhin and his team have identified a lead compound that reduces the levels of retinoid derivatives in the eye that are toxic to the photoreceptor cells. He believes it has the potential to be developed into a drug. With Harrington Discovery Institute support, he plans to finesse the medicinal chemistry to optimize the lead compound.

"Drug discovery is a very difficult process," Dr. Petrukhin notes. "It requires a diverse set of skills."

He speaks from experience. While at Merck, Dr. Petrukhin worked for many years on the genetics of macular degeneration in an attempt to identify drug targets for the purpose of inhibiting degeneration of the retina. Through that work he discovered two human disease genes responsible for two forms of inherited macular degeneration. He later transitioned from studying genetics of macular degeneration to developing pharmacological treatments for this blinding condition. One of his drug discovery projects at Columbia brought a drug candidate through the development process, and it now is approaching clinical trials.

Dedicated to his research, Dr. Petrukhin has little leisure time. When he is relaxing, he enjoys quiet time spent reading or listening to music. But even then, his research and self-imposed deadlines are never far from his thoughts. "My goal is to advance a new drug candidate developed specifically for a treatment of Stargardt disease to clinical trials within the life of the Gund-Harrington grant," he says. "There is much work to be done."

TECHNOLOGY with an Impact

To many people, the words “genetic engineering” conjure up scary images of mutant humans, super-sized steer and weird half-fish, half-mouse creatures.

For scientists like Donald Zack, MD, PhD, Co-Director, Johns Hopkins Center for Stem Cells and Ocular Regenerative Medicine, genetic engineering means almost boundless opportunities for advancing the treatment of genetic diseases.

Dr. Zack, who also is the Guerrieri Professor of Genetic Engineering and Molecular Ophthalmology at Johns Hopkins, is profoundly interested in the application of genetic engineering to the treatment of retinal disease such as retinitis pigmentosa (RP) and glaucoma. He is an expert in the use of CRISPR, a powerful, revolutionary technology that makes manipulating human DNA more accessible and less costly.

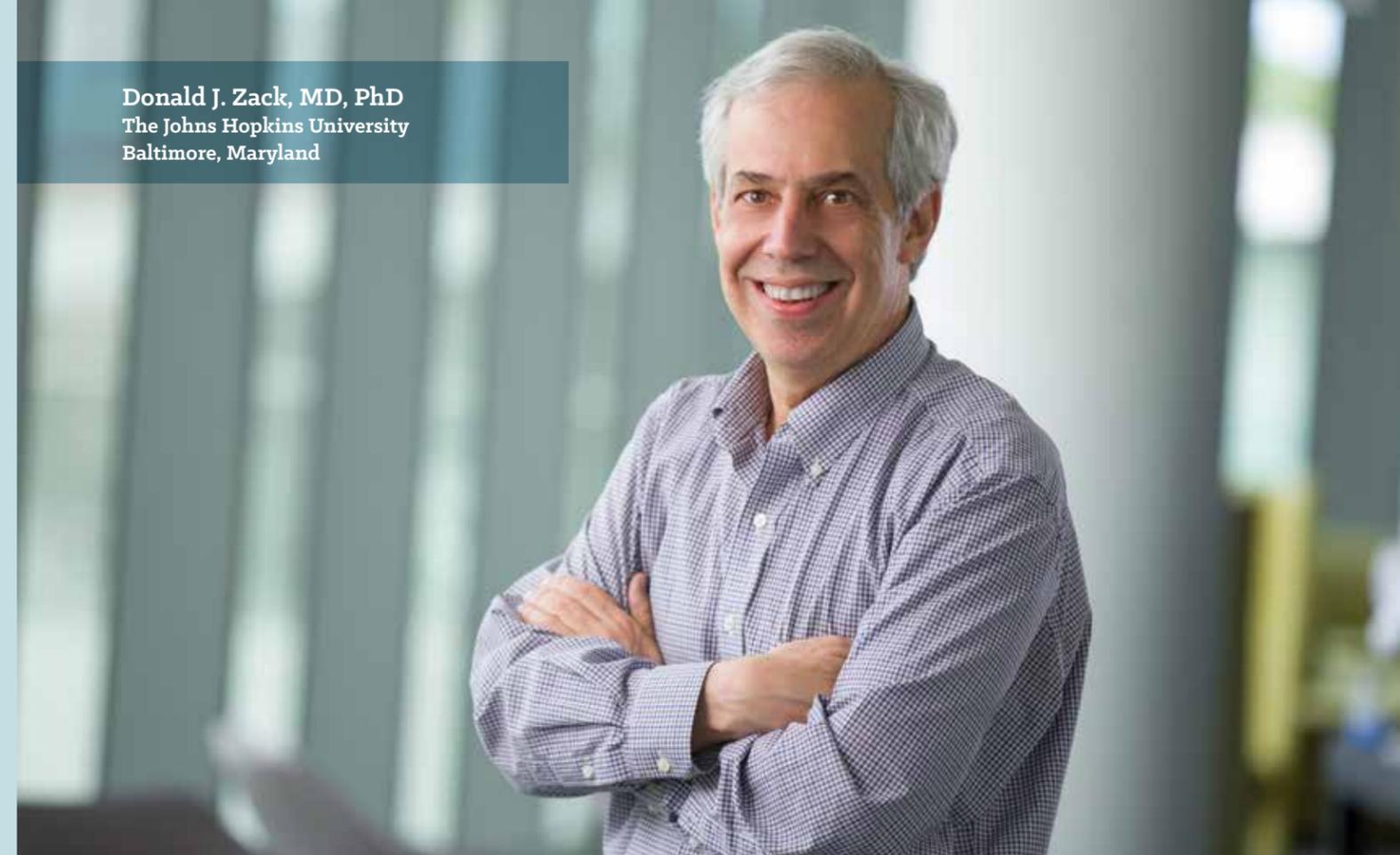
Dr. Zack has been dedicated to ophthalmology and the biology of the eye since his days as a student at the Albert Einstein College of Medicine. “The dean was leaving to go to the Massachusetts Eye and Ear Infirmary, and he was trying to recruit young scientists to bring new ideas to the study of eye disease,” Dr. Zack remembers. “I knew I wanted to pursue a career in medical research, and he sold me on ophthalmology.”

That decision set his future course. Now, after more than 30 years spent studying the eye, Dr. Zack believes he and his research team may be on the threshold of a treatment breakthrough for retinitis pigmentosa and other forms of retinal disease. They are applying CRISPR technology to develop methods to actually modify the DNA within a patient’s eye.

“We are putting together the pieces to get enough of the picture to at least understand and develop a treatment,” Dr. Zack notes.

Although Dr. Zack recently has given up his clinical ophthalmology practice to focus on research, his firsthand experience with individuals with retinal disease and the sufferings they endure are imprinted in his memory bank. “That’s what’s cool about this work; it combines basic science and the accumulation of knowledge with the clinical side,” he says. “If we can develop something to help patients, I would die happy.”

Donald J. Zack, MD, PhD
The Johns Hopkins University
Baltimore, Maryland



WHY THE BUZZ ABOUT CRISPR?

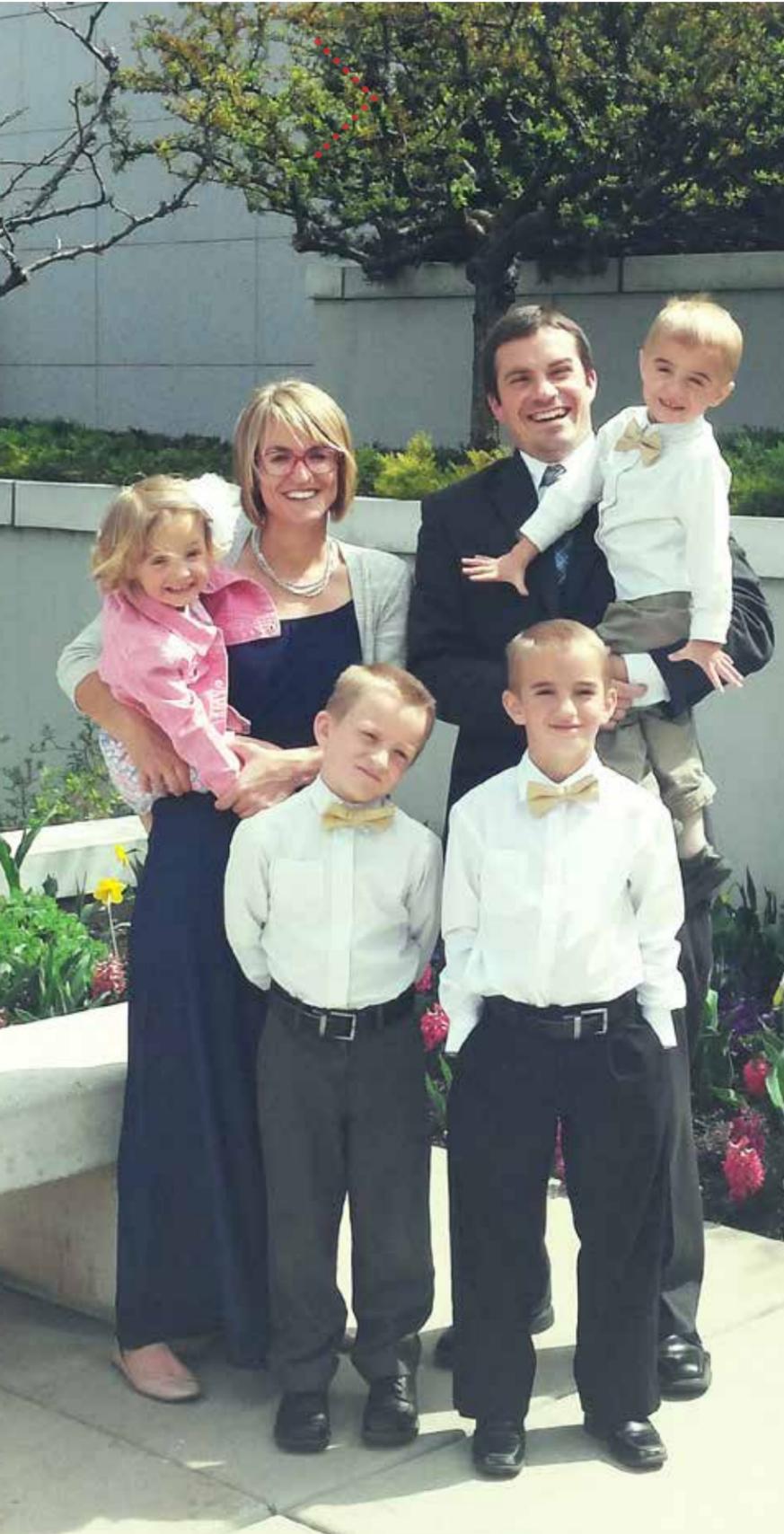
A Google search on CRISPR will yield more than 3 million results, nearly equally divided between lay press and scientific media. In the past three years, this revolutionary gene editing technology has captured the world’s imagination.

The CRISPR system originally evolved as a type of “immune system” in bacteria. However, clever human scientists have adapted it for far more interesting uses. CRISPR stands for “clustered regularly interspaced short palindromic repeats,” which describes a collection of short sequences in a cell’s DNA. Cas9 is an enzyme that cuts DNA. CRISPR-Cas9 makes altering genes relatively easy, inexpensive and fast and is more efficient and precise than earlier gene-editing technologies.

Cas9 can be engineered to cut DNA sequences at a precise location. The scientist designs the desired target sequence and orders a special short RNA molecule called a guide RNA (gRNA) that determines where the Cas9 enzyme cuts. The scientist “feeds” the gRNA target sequence along with the Cas9 enzyme to the desired cells. The Cas9 then uses its molecular scissors to make the cuts, and the scientist inserts a new genetic sequence into the genome.

This technique works in essentially any living being, from bacteria to farm crops to humans. Physician-scientists are excited about the potential CRISPR offers for molecular-based medicine – treating disease by slicing out and replacing genetic defects that cause conditions such as cystic fibrosis, retinal degeneration or muscular dystrophy. A number of companies have been formed that are planning to initiate human clinical trials using CRISPR within the next few years.

Genetic engineering is the process of modifying an organism’s genetic composition by transferring genes from one organism into a plant or animal of a totally different species.



Heartbreak and Courage: A Family's SCA7 Story

Most people have never heard of SCA7. For members of the Balling family, the disease has been a part of their lives for generations.

SCA7 (spinocerebellar ataxia type 7) is a rare, inherited disease characterized by progressive degeneration of the brain's coordination center and destruction of the rods and cones in the retina. People with SCA7 experience difficulty walking, swallowing and speaking. Vision at the eye's center declines, resulting in visual impairment and in some people, total blindness. Currently no effective treatment to slow symptoms or cure the disease is available anywhere in the world.

The story of a family with SCA7 is a story of loss. Loss of family members, motor skills, personal dignity. At 32, Mande Balling Hardie has been dealing with SCA7 symptoms, including decreasing vision, for 10 years, and throughout her life she has watched her loved ones suffer with and die from the disease.

Her mother, Cindee, died from SCA7 two years ago at age 56 after battling the disease for 28 years as it slowly robbed her of her mobility, communications and speech. Mrs. Balling was one of five siblings in her family who had the disease. Her brother died at 6 months of age from SCA7 and a sister at age 2 from the disease.

"My mother started having symptoms when my younger sister, Aubree, was born, and she knew exactly what it was," Mrs. Hardie says.

In the early '90s, the Ballings took their five children to the University of Utah to undergo a newly developed genetic test for SCA7. The test showed that Aubree and Mande had the genetic mutation for the disease, but their three older brothers did not.

Despite the disease's genetic component, its course is different for every individual. Mrs. Hardie first noticed her vision worsening when she was in college, where she roomed with her cousin who also had SCA7 and has since died. However, Aubree, 28, developed symptoms as a young teenager. Her disease has progressed much more rapidly, and she is wheelchair-bound. "Except for my sister, everybody in my family who had the disease is gone," Mrs. Hardie adds. "It is a long, drawn-out process."

When Mande and her husband, David, wanted to start their family, they were determined to do what they could to reduce the risk their children would inherit this horrific disease. The Hardies underwent preimplantation genetic diagnosis and in vitro fertilization, and consider themselves fortunate to have four healthy children, so far with no symptoms of SCA7.

The children, including a set of twins, are the light of Mrs. Hardie's life. Sadly, she remembers what it is like to have a mother with SCA7. "When she couldn't do things any more, she just loved us," she recalls with a catch in her voice. Not knowing what the future holds for her, David and their children, Mrs. Hardie only says she intends to do as much as she can as long as she can.

The Hardies, Aubree and the rest of the Balling family have been walking a difficult road together for many years. "There is no treatment, nothing you can do to help," Mrs. Hardie says.

But now the family has something important they did not have before – hope, in the form of Albert La Spada, MD, at the University of California, San Diego and a Gund-Harrington Scholar. Mande and Aubree's father, Richard Balling, a civil engineering professor at Brigham Young University, came across Dr. La Spada's name and body of work during his intensive research into SCA7. He was elated to learn that Dr. La Spada is pursuing a promising treatment for the disease. (See story on page 42.)

The family traveled from their home in Utah to California to meet with Dr. La Spada, and for the first time they felt optimistic about the future. "First, just the fact that he is studying our disease is amazing," Mrs. Hardie says. "And what he has found is amazing. With his drug, he can reverse the disease in mice. It's so promising."

Mande and Aubree are already enrolled in Dr. La Spada's SCA7 registry. By recording baseline measurements of people who have SCA7 and have symptoms, the registry creates a reference point for the clinical trials the sisters are eagerly anticipating.

"When they start testing Dr. La Spada's new drug, they will be able to mark our progress against baseline," Mrs. Hardie explains with a note of excitement in her voice.

"Dr. La Spada has given me hope where before I had none," she says. "Just the hope of what his drug can do is so amazing."

Mande Balling Hardie pictured with her husband, David, and their four children.



Ron Harrington Inducted into Horatio Alger Association of Distinguished Americans

The Harrington Project for Discovery & Development founder, Ronald Harrington, is a 2016 recipient of the Horatio Alger Award. Presented annually since 1947 by the Horatio Alger Association of Distinguished Americans, Inc., the award celebrates individuals who have succeeded despite facing adversity and who are committed to philanthropy and higher education.

Because of his business success and generous philanthropy, few people know that Mr. Harrington came from modest beginnings. He was born in 1942 in Baltimore, Maryland, the only child of a stay-at-home mother and a steel salesman father. When Ron was 7, his father died of a heart attack. Ron and his mother moved to Cleveland, where she found work as a secretary and Ron was cared for by an aunt.

After graduation from The Ohio State University with degrees in marketing and finance, Mr. Harrington eventually landed his dream job as a salesman for Lakewood, Ohio-based Bonne Bell Cosmetics Company. His mentor, Jess Bell, offered him ample opportunity, and Mr. Harrington soon rose to be the company's youngest sales manager. After Mr. Harrington suffered what likely was a heart attack (inconclusive), Mr. Bell encouraged Mr. Harrington to run, and he became an avid runner.

In 1977, Mr. Harrington joined his brother-in-law as co-owner of a manufacturing and distribution firm that served the restaurant and meat packing industries. They ran the business together for more than a decade. In 1990, Mr. Harrington purchased a distressed company that distributed ostomy supplies.

Focusing on details, teamwork and customers, Mr. Harrington, his wife, Nancy, and their two children, Ronnie and Jill, over time transformed Edgepark into an industry giant with 1,200 associates and 20 consecutive years of double-digit sales increases and profit growth. In 2007, The Jordan Company made a majority investment in Edgepark, and in 2013 Cardinal Health bought the company for \$2 billion.

In 2000, Mr. Harrington, still an avid runner, underwent quadruple bypass surgery at University Hospitals. The Harrington family has since focused its philanthropy on medicine and health

care. In 2008, the family established the University Hospitals Harrington Heart & Vascular Institute with a \$22 million gift. They followed this in 2012 with a \$50 million gift to establish The Harrington Project for Discovery & Development.

Through the Horatio Alger Association, the Harrington family's generosity will help support scholarships for high school students who want to go to college, show outstanding promise and demonstrate remarkable resilience in overcoming major challenges in their lives.

Mr. Harrington was inducted into the association in early April in Washington, DC. He joins a list of distinguished members who have made a difference in American business and society.

Mt. Sinai Foundation Gift Supports Harrington Discovery Institute Strategic Partnerships

The Mt. Sinai Health Care Foundation in September 2015 awarded a \$1 million grant to University Hospitals to catalyze the development of partnerships between Harrington Discovery Institute and national health research foundations.

The foundation's investment establishes the Mt. Sinai Health Care Foundation Fund, which assists the Harrington Discovery Institute with forming additional strategic partnerships at the national level. Ultimately, the Mt. Sinai Health Care Foundation anticipates that these alliances will strengthen Northeast Ohio as a hub of bioscience innovation and attract national peer organizations to the region.

The Mt. Sinai Health Care Foundation has long supported biomedical research in our region, and the organization considers it an area of grantmaking priority. Through the foundation's visionary health care philanthropy, it continues the biomedical research legacy of the now closed Mt. Sinai Medical Center, for which the foundation is named.

The Mt. Sinai Health Care Foundation has been a steadfast partner with UH for many years, supporting clinical research and education initiatives and helping launch programs to promote health within Greater Cleveland's most vulnerable communities. The foundation's grant to Harrington Discovery Institute is its largest gift to date to UH.

Burton D. Morgan Foundation Gift Encourages Mentoring for Scholars

Burton D. Morgan Foundation, a private foundation based in Hudson, Ohio, is dedicated to promoting entrepreneurship in Northeast Ohio. The Foundation is a leader in building the region's entrepreneurial ecosystem and has supported the advancement of the biomedical field through numerous grants to BioEnterprise over the past decade. Through its work in helping to craft a regional economic competitiveness strategy, the Foundation is keenly aware of the prioritization of the biomedical field as a significant cluster that is growing and contributing to the economic vitality of Northeast Ohio. The Foundation has followed the progress of Harrington Discovery Institute and BioMotiv with great interest since 2013.

In February 2016, the Foundation's interest was solidified with a financial commitment to Harrington Discovery Institute. Burton D. Morgan Foundation made a \$200,000 gift to University Hospitals to support the mentoring provided to physician-scientists by the institute's Innovation Support Center.

"We believe that our grant to the institute fits with our strategy to build a vibrant economy in Northeast Ohio through innovation and new ventures," Deborah D. Hoover, President and CEO of the Burton D. Morgan Foundation, explains. "The institute is helping physician-scientists gain expertise in the drug commercialization process and see the possibilities of their ideas."

Through this grant, the Foundation is providing biomedical entrepreneurs with the tools they need to develop sustainable ventures that add value, embody innovation and contribute to a healthy economy.

"We are mindful of the great strengths in biomedicine in this region, and we want to encourage groundbreaking efforts to bring important medical innovations to market," Hoover says.



Harrington family pictured with 2015 Harrington Prize for Innovation in Medicine recipient Douglas R. Lowy, MD.

Nature Magazine Highlights Role of Impact Philanthropists

Impact philanthropists Ron and Nancy Harrington were highlighted in a recent issue of Nature magazine, along with philanthropists Bill and Melinda Gates, and Facebook founder Mark Zuckerberg and his wife, Priscilla Chan.

The highly respected, international, peer-reviewed science journal featured Harrington Discovery Institute at University Hospitals – part of The Harrington Project for Discovery & Development – in an article about the role of impact philanthropy in supporting pioneering new models for advancing medicine for societal benefit.

The author notes that the Harringtons, like other notable philanthropists, share similar views on using philanthropy to address the most vexing biomedical problems – with the common goal of faster cures. The author also notes the unique model of The Harrington Project which pairs Harrington Discovery Institute, a nonprofit, with a mission-aligned for-profit, BioMotiv. Of special interest is the institute's Innovation Support Center network of

pharmaceutical industry drug development experts. That support is what most Harrington Scholars consider as the most valuable aspect of their collaboration with the institute.

“Harrington Discovery Institute and The Harrington Project are increasingly identified with enabling physician-scientists to improve the standard of care,” says Harrington Discovery Institute President Jonathan Stamler, MD. “To have this featured in Nature is further validation of the unique model we have created.”

In the Nature article, the author makes the case that Ron and Nancy Harrington's hands-on approach, like that of the Gates and Zuckerberg and Chan, is characteristic of impact philanthropists who work to make a major difference in the world.

Read the Nature article “Funding: Donor Drugs” online at <http://www.nature.com> or find it in Nature, volume 533, pp. S43 – S45, May 5, 2016.

2016 HARRINGTON SCIENTIFIC SYMPOSIUM Celebrates, Inspires Scholar-Innovators

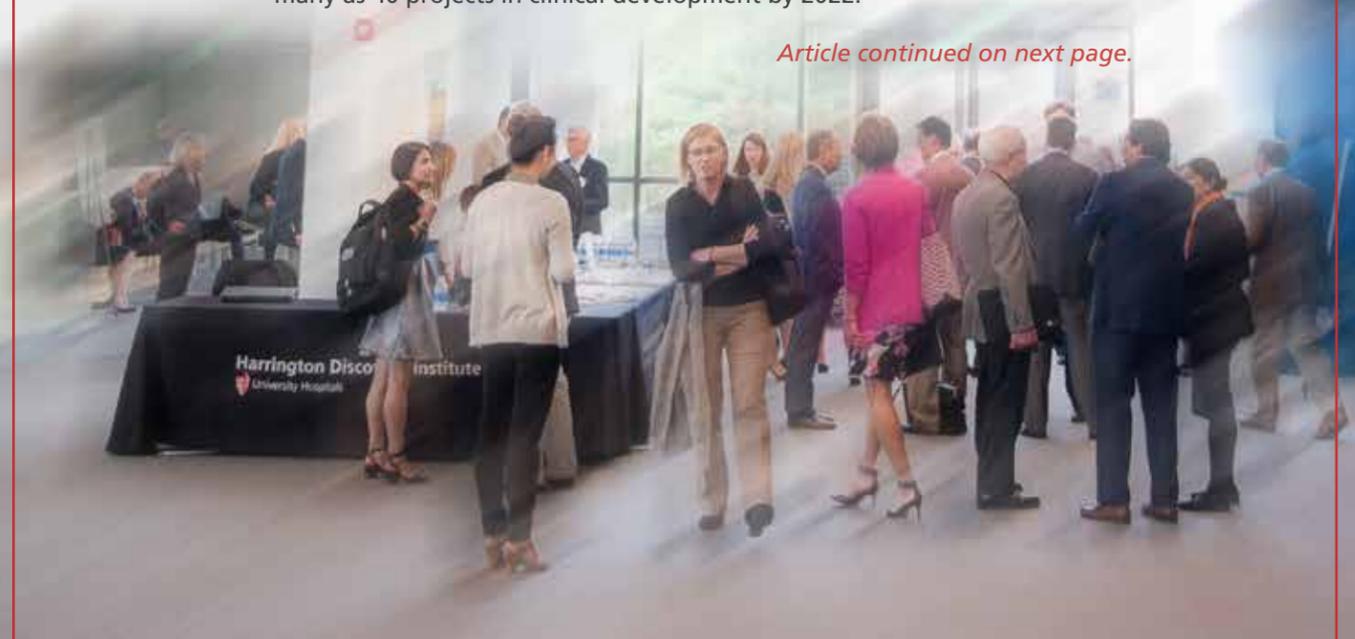
World leaders in science, medicine and academia gathered in Cleveland on May 25 – 26, 2016, to learn from and inspire their colleagues during Harrington Discovery Institute's 4th Annual Scientific Symposium. This year's symposium celebrated the remarkable momentum Harrington Discovery Institute has achieved in the four years since its founding.

Jonathan Stamler, MD, President, Harrington Discovery Institute, set the tone for the symposium on Wednesday afternoon when he referred to Harrington Discovery Institute as “nimble and ambitious.”

He noted that the institute now supports 57 physician-scientists, five Harrington Discovery Institute projects have transitioned to BioMotiv as startups, and three projects have attracted significant partnerships with major pharmaceutical companies. “This progress validates our model,” Dr. Stamler said. “We have demonstrated that when we say we will impact the future of medicine, we mean it.”

Harrington Discovery Institute founder Ron Harrington credited the institute's positive culture for encouraging and supporting discovery and innovation. “I am confident that we will achieve great things in medicine and society,” he said. “Like in business, I believe in working hard to move from good to great.” He predicted that Harrington Scholars may have as many as 40 projects in clinical development by 2022.

Article continued on next page.



Harrington Discovery Institute would like to extend a special thank you to our Scientific Advisory Board members whose expertise and deep commitment to our mission made the 4th Annual Harrington Scientific Symposium a resounding success:

David Ginsburg, MD, *James V. Neel Distinguished University Professor of Internal Medicine and Human Genetics, University of Michigan Medical School*

William G. Kaelin Jr., MD, *Professor of Medicine, Dana Farber Cancer Institute and Brigham and Women's Hospital, Harvard Medical School*

Beth Levine, MD, *Professor, Internal Medicine and Microbiology; Charles Cameron Sprague Distinguished Chair in Biomedical Science; UT Southwestern Medical Center*

Andrew R. Marks, MD, *Chairman, Department of Physiology and Cellular Biophysics, Columbia University Medical Center; Founding Director, Wu Center for Molecular Cardiology*

Charles Sawyers, MD, *Chairman, Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center*

Solomon H. Snyder, MD, DSc, DPhil, *Distinguished Service Professor of Neuroscience, Pharmacology and Psychiatry, Johns Hopkins University School of Medicine*

Michael J. Welsh, MD, *Roy J. Carver Chair in Biomedical Research, Professor of Internal Medicine, Molecular Physiology and Biophysics and Neurosurgery, University of Iowa*



Article continued from previous page.

Harrington Scholar-Innovators Nicole Calakos, MD, PhD, Associate Professor of Neurology and Neurobiology, Duke University School of Medicine (class of 2015), and Darren Carpizo, MD, PhD, Associate Professor of Surgery and Pharmacology, Rutgers Robert Wood Johnson University Medical School (class of 2014), shared personal insights on their experiences with the Innovation Support Center. Dr. Calakos and Dr. Carpizo credited their Innovation Support Center mentors with helping them navigate the path to commercialization for their drug discoveries. Dr. Calakos is developing a novel therapeutic for a rare movement disorder, and Dr. Carpizo's gene therapy for cancer has transitioned to BioMotiv and is the basis for a new company, Z53 Therapeutics, that will complete its development.

Winner of the 2003 Nobel Prize in Chemistry Peter Agre, MD, Bloomberg Distinguished Professor and Director, Johns Hopkins Malaria Research Institute at Johns Hopkins Bloomberg School of Public Health, completed Wednesday's agenda as keynote speaker with his presentation, "Opening

Doors Worldwide Through Medical Science."

A dinner at the historic Ballroom at Park Lane concluded Wednesday's events, honoring our Harrington Scholars. Attendees enjoyed the opportunity to hear personal reflections from Harrington Discovery Institute Scientific Advisory Board member Solomon H. Snyder, MD, DSc, DPhil, on his career as a physician-scientist.

The Thursday scientific sessions opened with brief reflections from Andrew I. Schafer, MD, on the challenges of a physician-scientist. He is Former Chairman of Medicine, Professor of Medicine, Director of the Richard T. Silver Center for Myeloproliferative Neoplasm, Weill Cornell Medical College, and well known as the author of "The Vanishing Physician-Scientist?" Dr. Schafer's optimistic remarks were a fitting prequel to the 2016 Harrington Scholar presentations that continued the symposium's momentum through the morning and afternoon.

During lunch on Thursday, Tadataka "Tachi" Yamada, MD, Venture Partner, Frazier Healthcare Partners, inspired the audience with his presentation "Lessons from Global Health." Dr. Yamada's

talk illuminated anecdotes from his personal experience as former President of the Bill & Melinda Gates Foundation Global Health Program, emphasizing the importance of urgency, innovation, measurement and partnerships in advancing medicine globally.

Dr. Yamada encouraged the audience to always consider a triage strategy of who will you allow to live and who will you allow to die. He pointedly questioned how many scientific papers are truly "revolutionary," given that millions of people still die of TB each year, an HIV vaccine does not exist and malaria treatment is more than 2,000 years old.

Further, Dr. Yamada stressed the importance of measuring the impact of research that already has been done. "As in tennis, if you're not keeping score, you are just practicing." In discussing the need for partnerships in innovation, Dr. Yamada noted, "No one can do it alone. There is a difference between invention and innovation. One must contemplate failure, as innovation and failure go hand in hand. And challenging dogma is a part of the ecosystem of innovation."

Through two days of networking, scientific meetings and stimulating presentations, the symposium fully engaged the Harrington Discovery Institute Scholars in Harrington Discovery Institute's mission: Accelerating breakthrough discoveries into medicine.

Harrington Discovery Institute will celebrate its fifth anniversary during the symposium on May 23 – 25, 2017.

"One must contemplate failure, as innovation and failure go hand in hand."

Dr. Tadataka Yamada
*Venture Partner
Frazier Healthcare Partners*

Dear Jonathan and Mukesh:

I want to thank you both so much for a wonderful experience with the Harrington Scientific Symposium recently. We as awardees were treated like royalty!

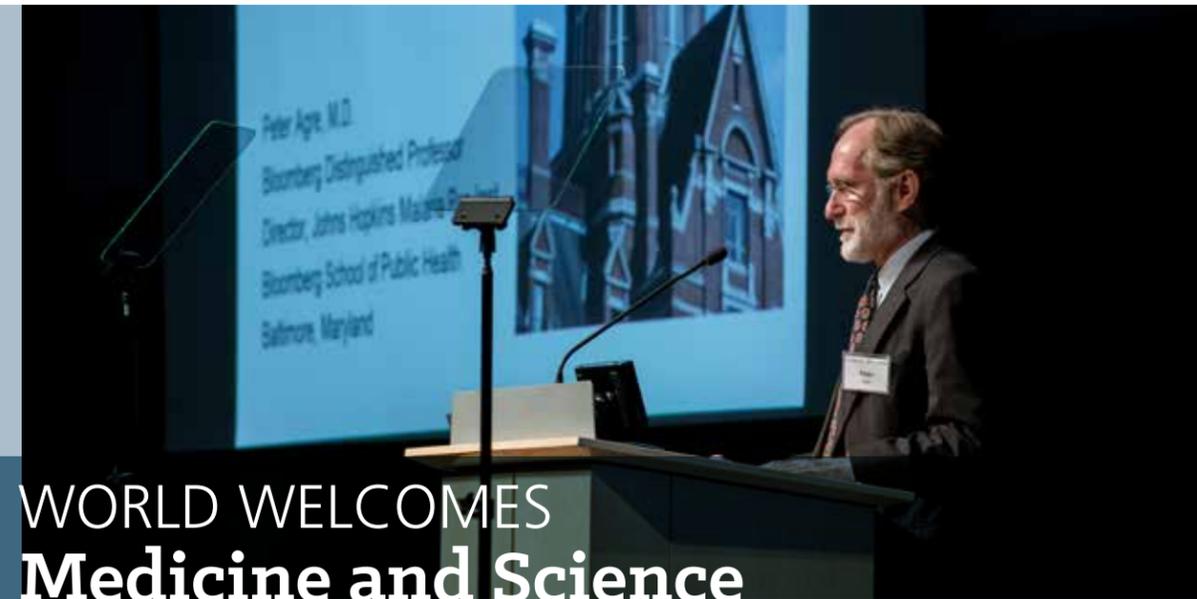
I certainly learned a lot, met some spectacular people for networking and really enjoyed all the talks. I will always have vivid memories especially of Dr. Tachi Yamada's inspirational talk that I have shared with many here at Pittsburgh. Meeting and chatting with Ron Harrington was wonderful as was with my team led by Perry Molinoff.

The HDI is truly a unique and remarkable operation, and I look forward to keeping you in the loop on our program.

Sincerely,

Rama

*(Rama K. Mallampalli, MD,
2016 Harrington Scholar-Innovator)*



WORLD WELCOMES Medicine and Science

The Fourth Annual Harrington Symposium welcomed Peter Agre, MD, Bloomberg Distinguished Professor and Director, Johns Hopkins Malaria Research Institute (JHMRI) at Johns Hopkins Bloomberg School of Public Health; Program Director, International Center of Excellence for Malaria Research; and winner, 2003 Nobel Prize in Chemistry, as keynote speaker Wednesday, May 25. Through his presentation, "Opening Doors Worldwide Through Medical Science," Dr. Agre engaged and inspired the audience with a recounting of his experiences in international public health and research with JHMRI.

The Johns Hopkins Bloomberg School of Public Health established JHMRI in 2001 to conduct basic-science research designed to treat and control malaria, develop a vaccine and find new drug targets to prevent and cure this deadly disease. Dr. Agre was recruited as Director in 2008, and JHMRI now comprises nearly two dozen malaria experts from around the world.

In 2003, Dr. Agre, who was a resident at University Hospitals in the 1970s, shared the Nobel Prize in Chemistry for his discovery of the aquaporin water channels. For more than a decade, his lab has focused on the role of aquaporins in malaria, such as the role of aquaglyceroporins as a pathway for glycerol transport, and the potential for exploiting aquaporins to treat or prevent the disease.

With his hallmark wit, Dr. Agre recounted his high school years in South Dakota as a "rebel," including disappointing his chemistry professor father by receiving a D in chemistry his senior year and ultimately dropping out. He turned serious, however, in discussing his dedication to saving the lives of children in developing countries, particularly Zambia and Zimbabwe.

"Despite ongoing efforts to control mosquito populations worldwide, malaria still causes a million deaths annually, most of them in children," Dr. Agre noted. He has seen firsthand in Africa the somber permanent effects of the disease such as blindness and brain injury in those children who survive malaria.

Dr. Agre's passion for preventing malaria in young children was evident as he shared numerous slides of beautiful, charming children in Zambia and Zimbabwe whom he has encountered in his work there. He recounted his team's remarkable progress in reducing the incidence of malaria in sub-Saharan Africa, particularly in the Macha region of Zambia.

The area is populated by traditional villagers, primarily members of the Batonga tribe, living in small, scattered homesteads where they survive by subsistence farming. Of the estimated 128,000 people in the Macha region, 50 percent of the population is under 12 years of age.

In 2000, the region recorded 1,479 cases of malaria and 106 malaria deaths. Over the past 15 years, Dr. Agre has made it his personal fight to impact those statistics. "Since 2000, JHMRI, in partnership with the Macha Malaria Research Institute in Zambia's Southern Province, has reduced the incidence of malaria in the country by 98 percent," he said.

In 2014, he reported, there were 26 cases and one death from malaria in the Macha region. "Our success is due to vaccination, screening and treatment, using the latest medicines that a typical Macha family could not otherwise afford," Dr. Agre said.

The JHMRI team continues basic and clinical research in malaria in both Zambia and Zimbabwe, focused on parasitology, entomology, immunization and vaccine development and epidemiology. Through an NIH grant that created the International Center of Excellence for Malaria Research, the team hopes to develop strategies for sustainable regional malaria control measures in these countries that address all aspects of this complex disease.

As President of the American Association for the Advancement of Science 2009 – 2010, Dr. Agre led science diplomacy missions to Cuba, North Korea and Myanmar (formerly Burma) where he met with national leaders and leading scientists and clinicians to lay the groundwork for future collaboration.

Dr. Agre believes in encouraging international scientific collaborations to address common human illness and diseases and to build positive international partnerships. "Medical science," he noted, "opens doors that otherwise would be closed to us, in countries that may have a less-than-favorable perception of the United States."



BioMotiv Ratchets Up THE MOMENTUM



As the mission-aligned biotech accelerator of The Harrington Project, BioMotiv has the goal of advancing discoveries into medicines and bridging research projects across to professional drug development organizations that can resource them for clinical and ultimately commercial development. BioMotiv's portfolio includes, but is not limited to, companies created around discoveries made by Harrington Scholar-Innovators.

In 2011, David U'Prichard, MD, a venture capitalist and former pharmaceutical company executive based in Philadelphia, had been working to raise a venture fund that would assemble a cadre of ex-pharmaceutical company executives like himself to manage an early-stage investment portfolio. Meanwhile in Cleveland, Ron Harrington, Harrington Discovery Institute President Jonathan Stamler, MD, and BioMotiv CEO Baiju Shah were working to form The Harrington Project and assemble a core group of experienced pharmaceutical developers to assist with technologies.

When the Harrington team met Dr. U'Prichard, the decision to work together was an easy one for everyone involved. "We immediately recognized that David's breadth of experience and networks would be beneficial to BioMotiv and the broader Harrington Project," Shah says.

Dr. U'Prichard agreed to come on board as BioMotiv's Chief Scientific Officer (CSO), Chair of the BioMotiv Advisory Board, and also a member of the BioMotiv Board of Managers. "Their emerging effort was very consistent with my thoughts about establishing a new model for innovation and drug development," Dr. U'Prichard says.

Dr. U'Prichard acquired his connections with major pharmaceutical companies and investors during a distinguished 35-year career spanning academic research, global R&D leadership, biotech company leadership, venture capital and board membership with pharmaceutical companies in the United States, United Kingdom, Europe and India, including positions as Global Head of Research at Zeneca and Chairman, R&D, at SmithKline Beecham.

Dr. U'Prichard began his work by assembling an impressive collection of former pharmaceutical industry executives to serve as team members for BioMotiv, and also referred individuals to work with Harrington Discovery Institute. He subsequently recruited several former heads of global R&D organizations to form the core of BioMotiv's Advisory Board. Among them are individuals who once led the R&D organizations of companies such as Johnson & Johnson, Wyeth, Forest Laboratories, Aventis and Warner-Lambert.

Dr. U'Prichard describes the BioMotiv Advisory Board as "the gateway in the diligence process that all new investment opportunities must pass through before being presented for investment to the Board of Managers."

BioMotiv's management team, led by Ted Torphy, PhD, who took over as BioMotiv's CSO in 2015, presents selected projects of potential interest to BioMotiv to the Advisory Board for diligence and review. The advisors are asked to review the scientific and business aspects of new opportunities. Dr. Torphy's role is to seek consensus among the Advisory Board members regarding an opportunity's scientific potential, business value, ability to address an unmet medical need, and fit for the BioMotiv development model, including its near-term partnering potential.

During the diligence process, an Advisory Board member is selected to act as the challenger to the management team. "We ask the advisors to kick the tires and question the choices that have been made," Dr. U'Prichard explains. "Going through this process is a way to force the best decision on every potential investment."

Projects that pass the Advisory Board's scrutiny and receive the support of the Advisory Board are then presented to the BioMotiv Board of Managers for investment. An affirmative vote adds the project to the corporate portfolio. BioMotiv then forms a "virtual" biotech company to develop the drug.

BioMotiv is responsible for establishing the leadership team, and, as the lead investor, funds the project in successive tranches when key milestones are passed. At any stage of this early development process, BioMotiv may partner with others to support the project, including universities, accelerators, investors, disease foundations and pharmaceutical companies.

As the biotech company develops and moves the drug through the development pipeline, the goal is to attract additional resource commitments to expand the effort and probability of success, including from pharmaceutical industry partners. For example, in January 2016, Dual Therapeutics, a BioMotiv portfolio company, announced a large collaboration with Bristol-Myers Squibb to advance small molecule compounds against an exciting new target for the treatment of different cancers and potentially other diseases.

BioMotiv's portfolio currently includes eight companies, with the potential to manage up to 20 at any given time. "We are expanding carefully as we establish our system and infrastructure, because we must remain responsible to our investors," Dr. U'Prichard notes.

That said, he adds that drug development ultimately is a numbers game. "Ron (Harrington) understands that BioMotiv must deliver many shots on goal," he says. "The more we do, the better our chances are statistically."

BioMotiv currently has \$135 million in capital under management.

THE HARRINGTON PROJECT
FOR DISCOVERY & DEVELOPMENT

BioMotiv

BIOMOTIV SPINOFFS AND PARTNERSHIPS

DLK 2013

Donald Zack, MD, PhD
Johns Hopkins
Retinal disease

Takeda 2014

Strategic partnership that confers to Takeda exclusive rights relating to programs sourced by BioMotiv
Immunology and oncology

Orca-Brickell Biotech 2015

Exclusive worldwide rights to RORy inhibitors
Topical treatment for psoriasis

Orca-AstraZeneca 2014

Strategic partnership
Oral medication for psoriasis, arthritis and other diseases that targets a protein involved in converting inactive immune cells into T-cells

Dual Therapeutics 2012

Goutham Narla, MD, PhD
Case Western Reserve University
Michael Ohlmeyer, PhD
Mount Sinai School of Medicine
Small molecule therapeutics for prostate cancer, lung cancer and acute lymphoblastic leukemia

Biogen 2015

Strategic partnership
Neurology and ophthalmology

Orca Pharmaceuticals 2013

Daniel Littman, MD, PhD
New York University
Oral drugs for the treatment of chronic inflammatory disease

Sujana Biotech 2015

Daniel Simon, MD
Case Western Reserve University
Edward Plow, PhD
Cleveland Clinic
Novel technologies and therapeutic products for a range of inflammatory and vascular disorders

Z53 Therapeutics 2016

Darren Carpizo, MD, PhD
S. David Kimball, PhD
Rutgers University
Anticancer drugs that target tumors with p53 mutations

Optikira 2015

Scott Oakes, MD
Feroz Papa, MD, PhD
University of California, San Francisco
Preventing accumulation of misfolded proteins, which leads to cell death in retinitis pigmentosa, diabetes, amyotrophic lateral sclerosis and other diseases

Charles River Laboratories 2016

Strategic development partnership

Dual Therapeutics-Bristol-Myers Squibb 2016

Strategic partnership
Small molecule therapeutics for prostate cancer, lung cancer and acute lymphoblastic leukemia

Arix Bioscience 2016

Strategic investment partnership

Allinaire Therapeutics 2016

Irina Petrache, MD
Matthias Claus, PhD
Indiana University
Target EMAP II protein in emphysema

Kodosil Bio 2014

Licensed from BioAlta to develop and commercialize the compound
IL-22 pathway directed antibody compound for the treatment of inflammatory and oncologic indications

Z53 ON THE FAST TRACK TO SUCCESS

Darren Carpizo, MD, PhD, a surgical oncologist at The Rutgers Cancer Institute of New Jersey, was named a Harrington Scholar-Innovator in 2014 for his research into mutation of the p53 gene, the most frequently mutated gene in human cancer. A p53 mutation disables the gene's normal mechanism for preventing cancer cells from multiplying.

"From over 30 years of research on p53, we know that it is one of the most important genes in cancer biology, yet we still do not have a drug available that

targets p53, although some are now in clinical trials," Dr. Carpizo says.

He and his team discovered one of the first drugs that targets mutant p53 and restores its cancer-killing properties. With the support of the Innovation Support Center, Dr. Carpizo was able to advance the drug closer to clinical trials.

In February 2016, BioMotiv and Rutgers University came together to form Z53 Therapeutics, a new biotechnology startup company that will develop anticancer drugs that target tumors

with p53 mutations. Z53 Therapeutics is based on intellectual property licensed from Rutgers University, developed from the laboratories of Dr. Carpizo and S. David Kimball, PhD, Associate Vice President, Research Translation and Commercialization, Rutgers Translational Sciences. Through Z53 Therapeutics, they will collaborate with Rutgers translational sciences experts to progress this emerging anticancer drug to testing in humans.

Allinaire Therapeutics CLOSING IN ON THE GOAL

When Irina Petrache, MD, then a pulmonary medicine specialist at the Indianapolis Richard Roudebush Veterans' Administration Hospital, was selected as a 2014 Harrington Scholar-Innovator, she had high hopes of expanding the treatment options for patients with chronic obstructive pulmonary disease (COPD).

She and her collaborator, Indiana University researcher Matthias Claus, PhD, had identified a protein in the body that causes inflammation and death of the cells that line the inside of blood vessels in patients with COPD. They patented the EMAP II protein as a

target in emphysema with the goal of formulating it as a drug and advancing it toward human testing.

Through Dr. Petrache's and Dr. Claus's efforts and input from Harrington Innovation Support Center mentors, EMAP II moved rapidly through the next developmental phases. Early in 2016, the BioMotiv board voted to add the project to the BioMotiv portfolio and, in April 2016, BioMotiv established Allinaire Therapeutics based on Dr. Petrache's work.

HARRINGTON SCHOLARS

2016 Harrington Scholar-Innovators

Nunzio Bottini, MD, PhD

La Jolla Institute for Allergy and Immunology

Stanley N. Cohen, MD

Stanford University

Benjamin M. Gaston, MD

Case Western Reserve University

Rama K. Mallampalli, MD

University of Pittsburgh

M. Peter Marinkovich, MD

Stanford University

David J. Milan, MD

Massachusetts General Hospital

Kevin D. Niswender, MD, PhD

Vanderbilt University

Susan P. Perrine, MD

Boston University

Ann Marie Schmidt, MD

NYU School of Medicine

Gerald I. Shulman, MD, PhD

Yale University

2015 Harrington Scholar-Innovators

Robert A. Bonomo, MD

Case Western Reserve University

John C. Burnett Jr., MD

Mayo Clinic

Nicole Calakos, MD, PhD

Duke University

David R. Clemmons, MD

University of North Carolina

Barry S. Collier, MD

The Rockefeller University

Clark W. Distelhorst, MD

Case Western Reserve University

Xianxin Hua, MD, PhD

University of Pennsylvania

Richard J. Johnson, MD

University of Colorado

Marikki Laiho, MD, PhD

The Johns Hopkins University

Geoffrey S. Pitt, MD, PhD

Duke University

Ira A. Tabas, MD, PhD

Columbia University

2014 Harrington Scholar-Innovators

Jayakrishna Ambati, MD

University of Kentucky

Darren R. Carpizo, MD, PhD

Rutgers Cancer Institute of New Jersey

Garret A. FitzGerald, MD

University of Pennsylvania

Mark S. Humayun, MD, PhD

University of Southern California

John N. Kheir, MD

Harvard University

Rahul M. Kohli, MD, PhD

University of Pennsylvania

Gavril W. Pasternak, MD, PhD

Memorial Sloan-Kettering Cancer Center

Irina Petrache, MD

National Jewish Health

David H. Rowitch, MD, PhD

University of California, San Francisco

Jean Y. Tang, MD, PhD

Stanford University

David Wald, MD, PhD

Case Western Reserve University

2013 Harrington Scholar-Innovators

Marc I. Diamond, MD

UT Southwestern Medical Center

Roger A. Greenberg, MD, PhD

University of Pennsylvania

Geoffrey C. Gurtner, MD, FACS

Stanford University

Richard N. Kitsis, MD

Albert Einstein College of Medicine

Wolfgang B. Liedtke, MD, PhD

Duke University

Sanford D. Markowitz, MD, PhD

Case Western Reserve University

Scott A. Oakes, MD

University of California, San Francisco

Feroz R. Papa, MD, PhD

University of California, San Francisco

Jonathan D. Powell, MD, PhD

The Johns Hopkins University

Larry S. Schlesinger, MD

The Ohio State University

Robert B. Wilson, MD, PhD

University of Pennsylvania

Harrington Distinguished Scholar (Early Career Award)

Goutham Narla, MD, PhD

Case Western Reserve University

2016 Alzheimer's Drug Discovery Foundation-Harrington Scholars

Travis L. Dunckley, PhD

Arizona State University

Sung Ok Yoon, PhD

The Ohio State University

2015 Alzheimer's Drug Discovery Foundation-Harrington Scholars

Carol A. Colton, PhD

Duke University

Jerri M. Rook, PhD

Vanderbilt University

2014 Alzheimer's Drug Discovery Foundation-Harrington Scholars

Thota Ganesh, PhD

Emory University

Chien-Liang Lin, PhD

The Ohio State University

2016 Gund-Harrington Scholar

David M. Gamm, MD, PhD

University of Wisconsin-Madison

2015 Gund-Harrington Scholars

Albert R. La Spada, MD, PhD

University of California, San Diego

Konstantin Petrukhin, PhD

Columbia University

Donald J. Zack, MD, PhD

The Johns Hopkins University

2016 Oxford-Harrington Scholar

Valentine Macaulay, MD, PhD

University of Oxford

2015 Oxford-Harrington Scholars

Helen McShane, MD, PhD

University of Oxford

Claudia Monaco, MD, PhD

University of Oxford

2014 Oxford-Harrington Scholar

Alison Simmons, MD, PhD

University of Oxford

For more information, visit HarringtonDiscovery.org

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