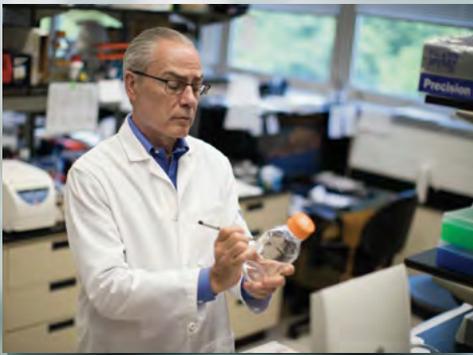


Harrington Discovery Institute

 University Hospitals | Cleveland, Ohio

BREAKTHROUGH DISCOVERIES THAT CREATE

IMPACT



2018-2019 ANNUAL PUBLICATION

DEAR COLLEAGUES,

In the seven years since the inception of The Harrington Project, our unique ability to more quickly and strategically shepherd scientific discoveries from bench to bedside has increasingly gained the attention of leaders within academia, healthcare and beyond.

Indeed, in the past year, recognition of the efficacy and influence of the Harrington platform led to launches of two exciting initiatives, which will enable us to direct powerful resources toward new areas of unmet therapeutic need:

- A first-in-kind relationship with the University of Oxford, that will align resources and expertise to improve treatment options globally for patients with rare diseases. The global Oxford-Harrington Rare Disease Centre will support the development of new treatments for rare diseases, one of humankind's most significant and unaddressed health challenges. The Cleveland Foundation showed its generous support for this joint program with a \$1 million grant.
- Through a new partnership with Morgan Stanley Global Impact Funding Trust (GIFT), we are transforming the way philanthropy supports the development of new medicines. *Morgan Stanley GIFT Cures powered by Harrington Discovery Institute* is a special interest program for philanthropists to amplify their impact by accelerating cures for multiple diseases.

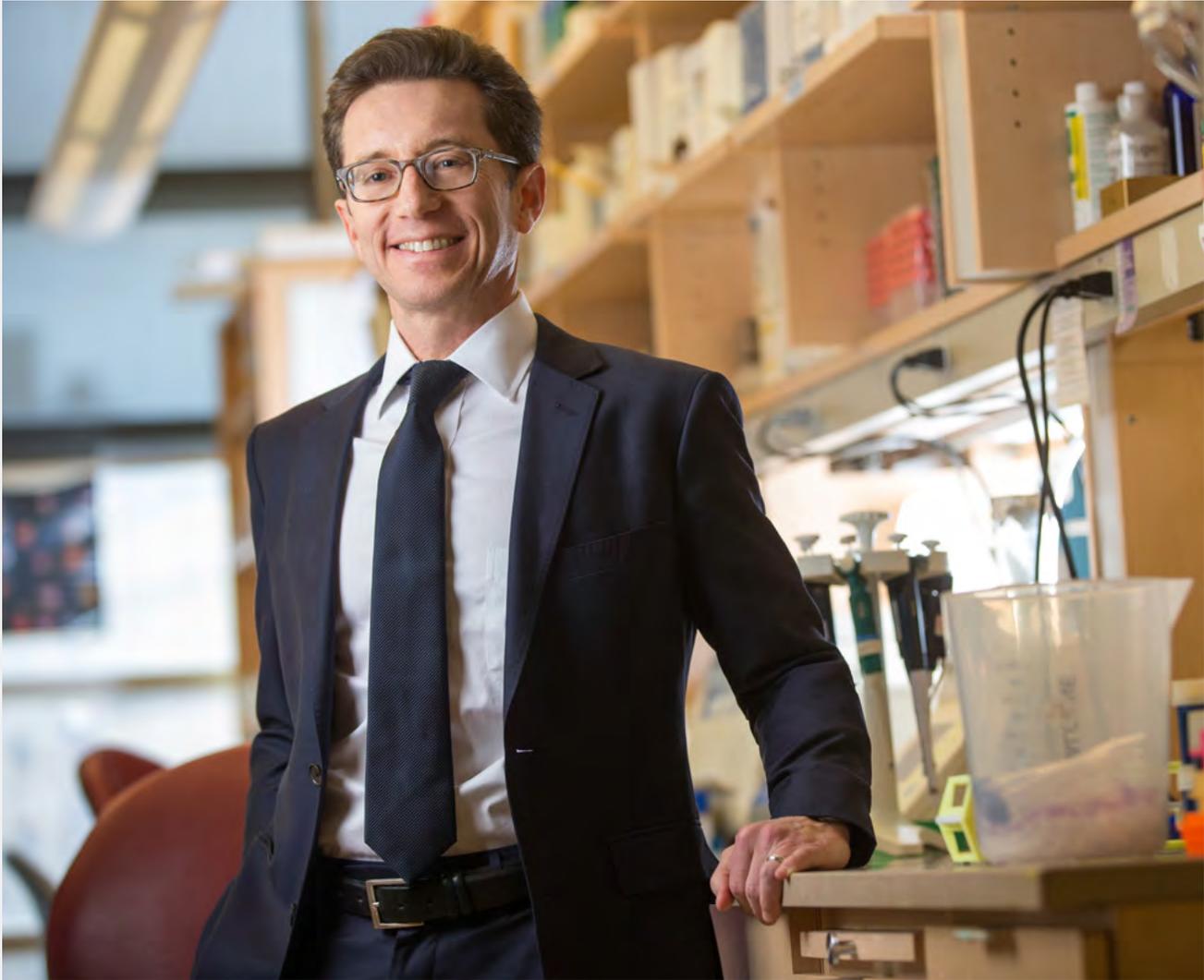
The original vision of the Harrington family—to create a more efficient and effective drug development model—has become more of a reality with each passing year. To date we have supported 110 Harrington Scholars from 50 institutions in their work to advance the standard of care for a wide range of diseases. By providing funding and drug development expertise, we are helping these brilliant scientists fulfill their common objective of accelerating research and therapies.

Just as important, we are prepared for the future. We have carefully constructed an operational framework designed to bear the weight of the changes that lie ahead, while remaining ever true to The Harrington Project mission.

I am excited for the future and the opportunity to positively impact the lives of individuals affected with disease.

Sincerely,





JONATHAN S. STAMLER, MD

President, Harrington Discovery Institute

Robert S. and Sylvia K. Reitman Family Foundation Distinguished Chair of

Cardiovascular Innovation, University Hospitals Cleveland Medical Center

Professor of Medicine and of Biochemistry and Director, Institute for Transformative

Molecular Medicine, Case Western Reserve University School of Medicine

FROM OUR SCHOLARS

“

PRACTICAL ADVICE ABOUT DRUG DEVELOPMENT that I never would have gotten from the academic world alone.”

“

Harrington Discovery Institute is MAKING SURE WE GET THIS RIGHT.”

“

My project team KNOWS WHAT IT TAKES TO GET AN INDUSTRY PARTNER INTERESTED in an invention.”

“

Harrington Discovery Institute is helping us FOCUS ON THE RIGHT EXPERIMENTS.”

“

Without the resources of the Harrington Discovery Institute I think I'D BE YEARS BEHIND.”

“

I have little knowledge of the pathway from discovery to development—that is a science itself, and Harrington has BROUGHT THAT EXPERTISE TO MY PROJECT.”

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A GROWING INNOVATION NETWORK

HARRINGTON SCHOLAR PROJECTS SUPPORTED TO DATE

Harrington Discovery Institute
University Hospitals | Cleveland, Ohio

THE HARRINGTON PROJECT MILESTONES ACHIEVED

110 DRUGS IN THE MAKING

50 INSTITUTIONS SUPPORTED

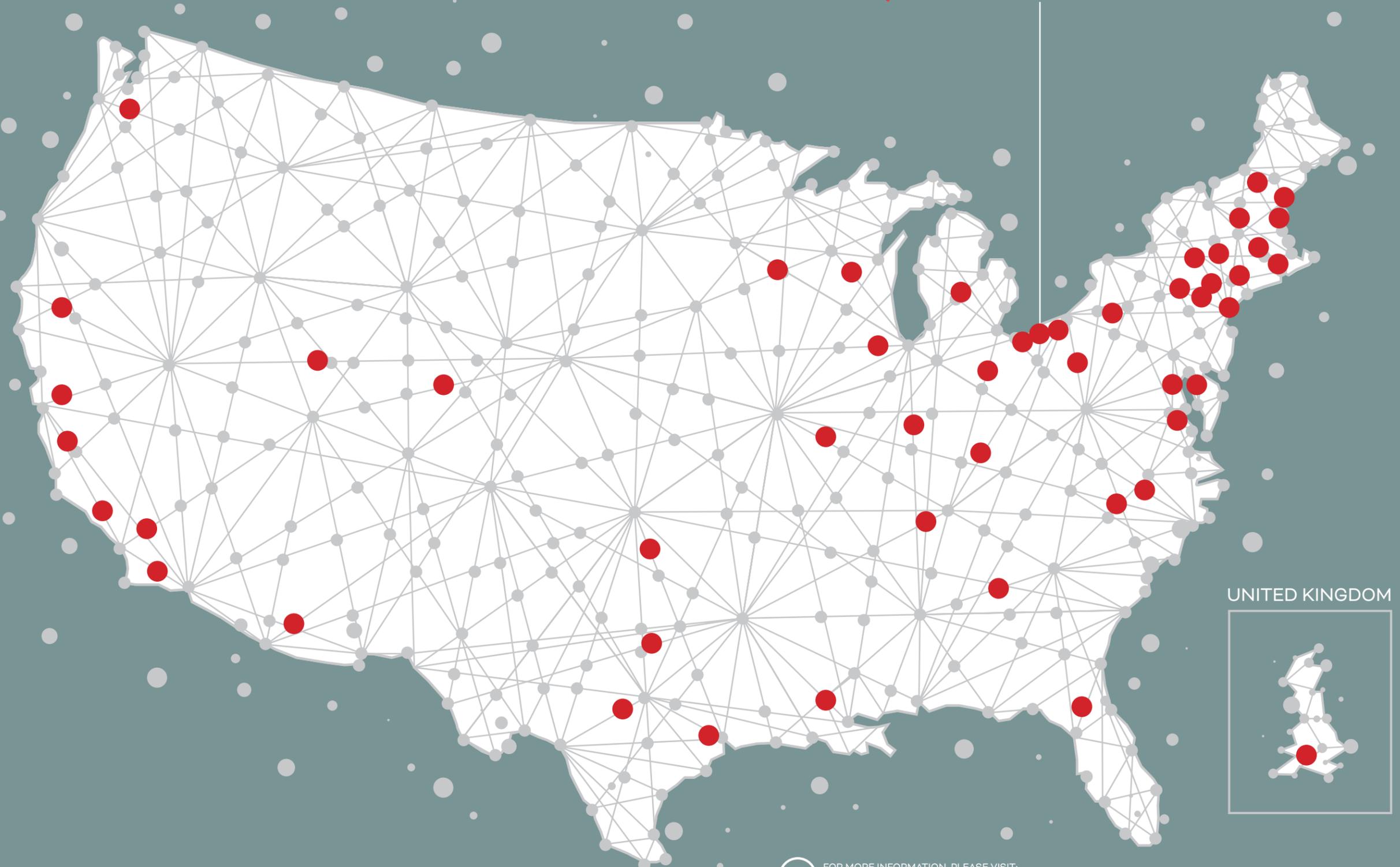
24 COMPANIES LAUNCHED

11 PROJECTS ADVANCED WITH OTHER COMMERCIAL SUPPORT*

7 MEDICINES IN THE CLINIC

6 MEDICINES LICENSED TO PHARMA

* NUMBER WILL FLUCTUATE AS PROJECTS PROGRESS



FOR MORE INFORMATION, PLEASE VISIT:
harringtondiscovery.org/Network



“There wasn’t anything like it in the world...seven years later, there still isn’t.”

RONALD G. HARRINGTON
Entrepreneur and Philanthropist

PHILANTHROPIC IMPACT

BEYOND MEASURE

Ron Harrington wasn't familiar with the phrase 'Valley of Death' when he was diagnosed with coronary heart disease almost 20 years ago. "When I had that health issue, that was right around the time when the Valley of Death—the market failure in drug development—really began to widen," Mr. Harrington says. "Realizing the magnitude of unmet medical need in the world—that hundreds of millions suffer from diseases with no cures or therapies, I began to think of ways to change, or perhaps circumvent, the problem."

In 2008, a sequence of events would lead to the Harrington family making a bold move to address the Valley of Death. They committed \$22 million to establish the Harrington Heart and Vascular Institute at University Hospitals, which led to a relationship with cardiologist Dr. Jonathan Stamler, an internationally renowned physician-scientist with three decades of drug development experience. Dr. Stamler and the Harringtons worked together to create a novel platform that would speed scientific discoveries into new medicines.

It was on an impact investment trip to Israel when Mr. Harrington knew with certainty they had an idea whose time had come. "We made twenty presentations to venture capital people, presidents of universities, and other Israeli leaders," he recalls. "Here's one of the most scientifically-advanced cultures in the world, and they could not find one thing wrong with our model. We came back to the States and said, 'we have something here.'"

In 2012, the Harrington family made a \$50 million gift to University Hospitals, and The Harrington Project for Discovery & Development was created.

"We have helped enable and further progress on crucial scientific work in many disease areas," Mr. Harrington says. "What has been interesting is that over the past three years, as people and entities reach out to us with unmet needs, we've seen an increasing emphasis on rare diseases—in part because these diseases are being found faster than medicines can be created."

The Harrington Discovery Institute is entering its second year collaborating with Takeda Pharmaceuticals on a Rare Disease Scholar program, and has established the Oxford-Harrington Rare Disease Centre in partnership with the University of Oxford.

2018 also marked the beginning of a relationship with Morgan Stanley's Philanthropy Management Group. "Morgan Stanley really understood what The Harrington Project is all about, and we're excited to be working with an institution that has the ability and resources to help us make dramatic differences in people's lives everywhere," Mr. Harrington says.

"Our family is thrilled to see the incredible growth of The Harrington Project in only seven years. We've done it with a great, game-changing idea, very smart people, and a culture founded on the most noble of aims; to cure people. Who wouldn't want to be a part of that?"

FIRST, AN IDEA.

THEN EXCELLENCE

The Harrington Discovery Institute, part of The Harrington Project for Discovery & Development, began with a strong focus on advancing discoveries made by physician-scientists into medicines to benefit society.

“The focus on physician-scientists was because these individuals, by virtue of their engagement in both patient care and research, are particularly focused on translating discoveries as a core part of their mission,” said Mukesh K. Jain, MD, Chief Scientific Officer, Harrington Discovery Institute. “We made a presentation about Harrington Discovery Institute to the American Society for Clinical Investigation (ASCI) in April, 2012, when it was virtually unknown,” Dr. Jain recalls. “The ASCI membership represents the creme de la creme of physician-scientists in the country and was certainly the right target audience. That was a good start.” Indeed, over the past seven years since inception, nearly 50% of the Scholar-Innovator awardees are ASCI members.

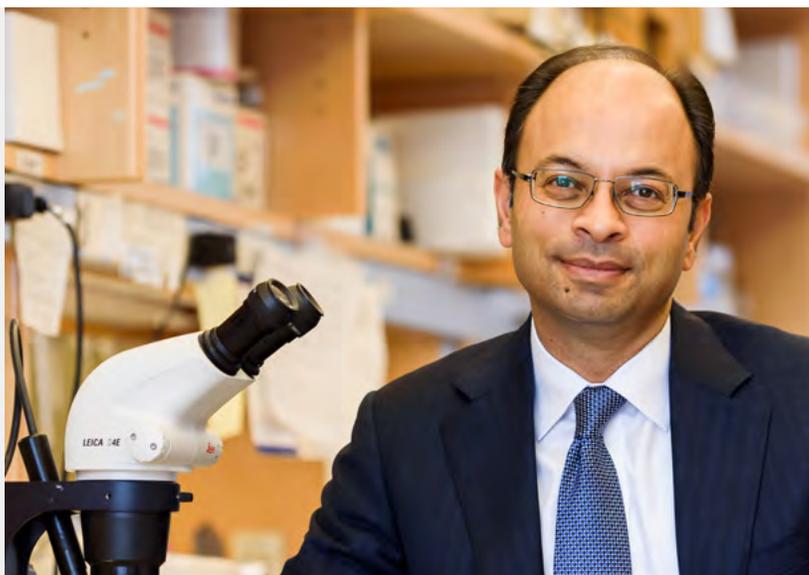
With the launch of its inaugural Scholar-Innovator program and an outstanding Scientific Advisory Board in place, Harrington Discovery Institute was beginning to be recognized as an organization committed to supporting the nation’s physician-scientist community.

“As we gained traction, we decided a few years later to tackle a second challenge facing the physician-scientist community—the lack of a supportive home in academia,” said Dr. Jain. Over the past several decades, the shifts in the healthcare landscape have resulted in hospital departments becoming more focused on patient volume and revenue. And since basic science departments have historically focused on pure discovery, the physician-scientist has increasingly found him/herself without a proper home and critical mass of like-minded individuals. “Jonathan and I are both very proud of our physician-scientist identity and decided that perhaps developing an onsite community of physician-scientists to complement our national efforts might

be a worthwhile initiative,” noted Dr. Jain. The first Harrington Investigator recruited was Andrew A. Pieper, MD, PhD, who joined Harrington Discovery Institute in early 2018. Given his extensive background in neuroscience, he also assumed the leadership of the Alzheimer’s Drug Discovery Foundation and Foundation Fighting Blindness scholar programs. With the growing focus on rare disease, the Institute then recruited geneticist Atul Chopra, MD, PhD, who joined in July 2018 as Associate Director of the Harrington Rare Disease Program. “I think what we have created is an ideal environment for physician-scientists interested in translating their fundamental discoveries into therapies,” said Dr. Jain.

“We are still a small physician-scientist community, but we are committed to growing significantly over the next few years. These efforts will enrich our local biomedical ecosystem and perhaps even serve as a role model for other organizations to develop programs dedicated to physician-scientists,” said Dr. Jain.

MUKESH K. JAIN, MD
Chief Scientific Officer,
Harrington Discovery Institute



THE 2018 HARRINGTON PRIZE FOR INNOVATION IN MEDICINE



A MUTATION THAT LED TO **LIFE-SAVING DRUGS**

HELEN H. HOBBS, MD

Director, Eugene McDermott Center
for Human Growth and Development
Professor of Internal Medicine and Molecular Genetics
University of Texas Southwestern
Investigator, Howard Hughes Medical Institute

No one knew precisely what factors controlled blood cholesterol levels. Then Helen Hobbs came along. Dr. Hobbs' discovery of a new gene that determined cholesterol levels led to the swift development of a drug to prevent heart disease, and her research changed the methodology used by many genetic researchers.

At the University of Texas Southwestern (UTSW) in the early 1970s, scientists discovered the low-density lipoprotein (LDL) receptor, which controls the level of cholesterol in the blood and in cells. This Nobel Prize-winning discovery led to the development of statins, which help reduce the effect of the accumulation of harmful fats in the circulatory system.

But since then, aside from statins, there has only been lifestyle advice: don't smoke, avoid fatty foods and food with a lot of bad cholesterol, exercise regularly.

In the early 1980s, after completing an internship in internal medicine at Columbia-Presbyterian Medical Center and her residency at UTSW, Helen Hobbs began working as a postdoctoral fellow with Drs. Michael Brown and Joseph Goldstein in that same UTSW molecular genetics lab. But she found it challenging to shift from solving multiple medical issues every day at a hospital, to research, with its slow experimental march toward scientific understanding. Fortunately for her, and for the world of healthcare, one particular scientific puzzle captured her interest.

"They had a collection of samples from children with very high cholesterol levels and heart attacks at an early age due to mutations in the LDL receptor gene," Dr. Hobbs recalls. "My first project was to characterize the nature of the LDL receptor mutations. I identified a deletion in a gene that was particularly common in individuals of French-Canadian ancestry. Why would so many unrelated people in Quebec province have the same mutation? It was uncovering the story behind this that sparked my interest in human genetics." (She discovered that all those people had ancestors from the same small region in France.)

After starting her own lab, she established a population-based study to discover new sequence variations that contribute to the

*“It’s just so thrilling to discover something new.
For these people, this PCSK9 drug is a life-saver.”*

susceptibility (and resistance) to heart disease. Dr. Hobbs’ team of scientists sent 50 people out to knock on doors in Dallas and enroll individuals into the study, in which participants would visit a clinic where detailed imaging studies would be performed. Blood was collected to measure proteins and lipids and to isolate DNA. A database was developed that included all the information collected on each of the 3,557 participants.

At that time, it was still not clear what role a high LDL played relative to other risk factors in the development of heart disease. Perhaps people with higher levels of LDL have more heart disease because they eat a poor diet, or don’t get enough exercise—rather than because of the high levels of circulating cholesterol. “A lot of people didn’t think LDL levels were a major causative factor in most people,” Dr. Hobbs says.

Four years later, when a geneticist in France found a connection between families with high rates of heart disease and a newly identified gene called PCSK9, Dr. Hobbs and her scientific partner Jonathan Cohen, PhD, hypothesized that other types of mutations in PCSK9 might lower plasma cholesterol levels.

Sure enough, she and Dr. Cohen found that two percent of African-Americans in Dallas had a mutation in PCSK9 that inactivated the protein, an anomaly that correlated with a markedly lower plasma cholesterol level. They discovered that this group was protected from heart disease, despite many having multiple cardiovascular risk factors like smoking, diabetes, and hypertension. This observation revealed the primacy of high cholesterol in the genesis of heart attacks.

They went on to provide new insights into the role of PCSK9 in cholesterol metabolism, which led to the rapid development of two FDA-approved therapeutic agents that lower cholesterol levels and reduce the risk of heart disease.

These remarkable findings also earned Dr. Hobbs the \$3 million Breakthrough Prize, the largest award in the sciences. More importantly, the discovery of this single genetic trait led to the development of a new strategy to prevent heart disease.

Dr. Hobbs, Director of the Eugene McDermott Center for Human Growth and Development, received her MD from Case Western Reserve University in 1979. Dr. Hobbs is an Investigator of the Howard Hughes Medical Institute.



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.



TO LEARN MORE ABOUT THE HARRINGTON PRIZE, PLEASE VISIT:
harringtondiscovery.org/Prize



ANDREW A. PIEPER, MD, PhD
Harrington Investigator
Director of Neurotherapeutic Discovery

A TOP NEUROSCIENTIST WHERE, AND WHEN, **HE'S NEEDED MOST**

If it is fair to say that the most reliable measure of an institution's importance is the willingness of the top experts in its field to join it, then the Harrington Discovery Institute has officially become a singular force in the cause of improving human health.

When Andrew A. Pieper, MD, PhD, moved his lab to Cleveland from the University of Iowa in 2018, University Hospitals and Harrington Discovery Institute welcomed one of the nation's leading physician-scientists in the field of neuropsychiatric disorders.

He now serves as the Director of Neurotherapeutic Discovery, a role in which he is currently overseeing the Alzheimer's Drug Discovery Foundation-Harrington

Scholar Program and the Gund-Harrington Scholar program.

Dr. Pieper earned his PhD in Neuroscience under the mentorship of Dr. Solomon Snyder, one of the most highly cited researchers in the biological and biomedical sciences, and whose work has led to many fundamental advances in molecular neuroscience.

"Sol challenges his students to pursue bold questions with the potential for one day improving the lives of patients, and his passion for scientific discovery energizes everyone around him," Dr. Pieper says.

"The privilege of having trained under Sol's mentorship is something that I will treasure the rest of my life."

As a Harrington Investigator, Dr. Pieper strives to identify and pursue important biological insights into neuropsychiatry, with particular focus on neuro-degeneration in disease, injury, and normal aging. He is committed to forging a path to new therapies for patients suffering from currently incurable or difficult to treat neuropsychiatric disorders.

"Big pharma hasn't been successful at finding new therapies for the wide array of neurodegenerative diseases facing society," Dr. Pieper says. "With people living longer, this is rapidly becoming a worldwide crisis that needs to be directly addressed."



TO LEARN MORE ABOUT THE HARRINGTON INVESTIGATOR PROGRAM, PLEASE VISIT:
harringtondiscovery.org/Investigator

PIEPER LAB MEMBERS:
 Seated, left to right: **MIN-KYOO SHIN, PREETHY SRIDHARAN, CORAL CINTRON-PEREZ;**
 Standing, left to right: **YEOJUNG KOH, KATHRYN FRANKE, KALYANI CHAUBEY, ANDREW PIEPER, EDWIN VAZQUEZ-ROSA;**
 On Stairs, lower to upper: **MATASHA DHAR, MALLORY LONG, EDWIN PACHECO-COLON**



WORKING AT THE CORE OF WHAT MAKES US HUMAN

The Pieper laboratory is composed of scientists at all levels working together to discover new ways to improve brain health, coordinated by the leadership of lab manager Coral J. Cintrón-Pérez, MBA.

Min-Kyoo Shin, PhD, Edwin Vazquez-Rosa, PhD, and Matasha Dhar, PhD are all senior research associates working on identifying unique pathological events related to nerve cell death, metabolism, and self-repair of nerve cells under conditions of injury, disease, and normal aging.

Kalyani Chaubey, PhD, a research associate, is identifying novel changes in nerve cell protein expression under these same conditions, with the goal of identifying new signaling pathways

that could provide new therapeutic opportunities for patients.

Edwin Pacheco Colón, MS, MBA, Yeojung Koh, BA, and Kathryn Franke, BA are laboratory technicians working on various projects, including identification of novel blood-based biomarkers of neurodegeneration to help guide clinical trials and also provide insights into fundamental processes in neurodegeneration.

Mallory Long, BA is a Neuroscience graduate student studying the role of brain blood vessels in brain health. Preethy Sridharan, BA, is a Medical Scientist Training Program (MSTP) student investigating the therapeutic potential of augmenting peripheral gasotransmitter signaling in brain health.

A MAJOR GRANT TO HELP KEEP AGING BRAINS HEALTHY

Dr. Andrew Pieper is co-director of a \$9.6 million grant, entitled *Restoring the Neurovascular Unit*, awarded to three members of Harrington Discovery Institute at University Hospitals for their research into brain health related to aging. This funding from the American Heart Association-Allen Initiative in Brain Health and Cognitive Impairment will help these researchers identify new ways to protect people from cognitive decline.

More specifically, the Harrington Discovery Institute team will work to better understand the interface between the cardiovascular system and the brain, known as the neurovascular unit. This interface is where the blood vascular system terminates in the brain, and is composed of cells from both the brain and the

vasculature. At this location, these cells interact in unique ways distinct from their separate functions elsewhere in the brain and vascular system.

“As we age, our brains are increasingly susceptible to a number of different conditions, including Alzheimer’s disease,” Dr. Pieper says. “Our goal is to meaningfully advance our basic understanding of the physiological role of the neurovascular unit in brain aging and dementia, as well as to provide new opportunities for therapeutic intervention. Learning more about the unique physiology at the neurovascular unit will help us discover new ways to protect our brains from neurodegenerative diseases linked to aging.”

With the naming of its newest class of Scholar-Innovators, Harrington Discovery Institute has now supported 110 scholars since 2012. The 2019 Harrington Scholar-Innovator awards support breakthrough innovations in diverse research areas including metabolic disorders, cancer, autoimmune disorders and parasitic diseases.

100+

THE 2019 HARRINGTON SCHOLAR-INNOVATOR AWARD RECIPIENTS:

ROBERT E. ANDERSON, MD, PhD

University of Oklahoma

PENG JI, MD, PhD

Northwestern University

ROSA BACCHETTA, MD

Stanford University

V. VINOD MOOHA, MD

University of Texas Southwestern

GERALD W. DORN, II, MD

Washington University

DAWN M. WETZEL, MD, PhD

University of Texas Southwestern

JOACHIM HERZ, MD

University of Texas Southwestern

T.C. WU, MD, PhD

The Johns Hopkins University

PAUL W. HRUZ, MD, PhD

Washington University

ELLEN YEH, MD, PhD

Stanford University



TO LEARN MORE ABOUT THE 2019 HARRINGTON SCHOLAR-INNOVATORS, PLEASE VISIT:
harringtondiscovery.org/2019SI

HARRINGTON SCHOLAR PROGRAMS

HARRINGTON SCHOLAR-INNOVATOR AWARD

This award recognizes physician-scientists whose research has the potential to change the standard of care. Each year, the Harrington Discovery Institute's Scientific Advisory Board reviews applications from outstanding physician-scientists and selects those whose discoveries embody innovation, creativity and potential for clinical impact.

ELIGIBILITY: MD OR MD/PHD IN THE U.S. OR CANADA (ADDED IN 2019)

ADDF-HARRINGTON SCHOLAR AWARD

In partnership with the Alzheimer's Drug Discovery Foundation (ADDF), the award supports research efforts that seek to prevent, treat, or cure Alzheimer's disease, related dementias and cognitive-decline associated with aging.

ELIGIBILITY: MD OR PHD IN THE U.S. OR CANADA (ADDED IN 2019)

GUND-HARRINGTON SCHOLAR AWARD

In partnership with Foundation Fighting Blindness, the award supports innovative researchers who seek to translate their findings in retinal degenerative diseases into new therapies to improve and/or restore vision.

ELIGIBILITY: MD OR PHD IN THE U.S. OR CANADA

HARRINGTON RARE DISEASE AWARD

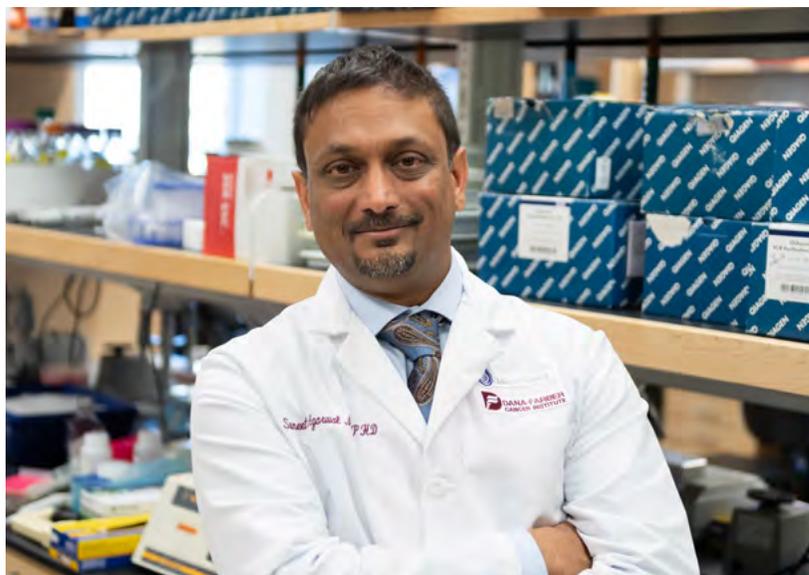
This two-year program is sponsored by Takeda Pharmaceutical Company Limited. The award provides support to researchers whose discoveries show promise for translation into novel medicines for rare diseases. The inaugural class was selected in 2018 and will be announced in 2019. Learn more about the Takeda-Harrington collaboration on page 39.

ELIGIBILITY: MD OR PHD IN THE U.S.



TO LEARN MORE ABOUT SCHOLAR PROGRAMS, PLEASE VISIT:
harringtondiscovery.org/FundingandPrograms

SUNEET AGARWAL, MD, PhD
Assistant Professor of Pediatrics
Harvard Medical School
Co-Program Leader for the
Stem Cell Transplant Center
Dana-Farber Cancer Institute and
Boston Children's Hospital



ANOTHER PLEASANT SURPRISE IN THE GENOME ERA

FOCUS: Preventing dyskeratosis congenita (DC) and idiopathic pulmonary fibrosis (IPF) by restoring levels of a specific RNA molecule, as well as telomere homeostasis, in patient cells.

Telomeres are caps at the ends of chromosomes that regulate how many times cells can divide. Problems that lead to diseases such as DC and IPF arise when there are mutations in the genes that regulate telomere biology. Dr. Agarwal's team appears to have found that when the PAPD5 enzyme is inhibited, telomere homeostasis in cells from IPF and DC patients is restored.

But that's only the beginning. Once you have agents that target fundamental pathways, often there are other conditions to which

your approach will apply. "We anticipate that these studies will yield novel telomerase modulators that could be useful in pulmonary fibrosis, bone marrow failure, and a range of degenerative disorders," Dr. Agarwal says. "Such links are increasingly being made, and validate focused efforts on rare diseases."

"I met DC patients at a family camp about eight years ago, and decided I wanted to fix this disease," Dr. Agarwal says. "The possibility of coming up with a breakthrough treatment for it is very

exciting. So is the notion that our work is leading to a broader body of knowledge that will apply to other diseases."

With support from Harrington, Dr. Agarwal is pursuing the goal of identifying small molecule modulators of PAPD5 activity, then testing their impact on telomere biology in patient cells.

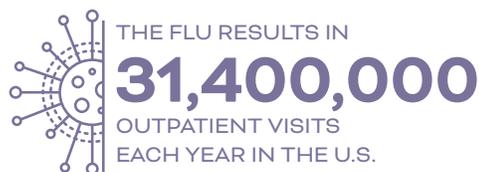


FOR MORE INFORMATION, PLEASE VISIT:
harringtondiscovery.org/Videos

IMPACT WISH:

"We have high hopes that our work will yield novel telomerase modulators that could be useful in pulmonary fibrosis, bone marrow failure, and a range of degenerative disorders."

THE RUSH TO PREVENT A PANDEMIC



FOCUS: *Developing a universal therapeutic that can prevent as well as treat all strains of influenza A.*

When the topic is potential worldwide viral epidemics, Dr. Glenn is in a position to see the big picture—due to what he sees at the molecular level. “Influenza A virus (IAV), to name just one, presents in a constantly changing and wide range of strains and subtypes that cause disease, ranging from seasonal flu to lethal pandemics capable of killing millions,” Dr. Glenn says.

Moreover, strains can quickly develop resistance to neuraminidase inhibitors (NAIs) such as Tamiflu. But there’s an even more alarming prospect to consider. “Strains can now be easily designed to cause disease—in fact, my graduate student could design an influenza virus that could kill 100,000,000 people, and vaccines offer no protection against such threats,” Dr. Glenn says.

To target viruses and prevent virus drug resistance, Dr. Glenn has focused on RNA secondary structures, which are formed when RNA genetic material folds on itself into specific shapes.

“Often in viruses, the secondary structures encode critical regulatory signals,” he says. “Secondary structures are often highly conserved; so I thought that if a drug could be designed to target an essential RNA secondary structure, the structure would have limited ability to mutate and escape from the drug. If so, this could translate to a high barrier to the development of resistance to the drug.”

Harrington Discovery Institute is helping Dr. Glenn pinpoint the optimal target, develop a potent, long-lasting compound, and help develop the compound into a new drug for the clinic.



JEFFREY S. GLENN, MD, PhD

Professor of Medicine (Gastroenterology and Hepatology) and of Microbiology and Immunology
Stanford University School of Medicine

IMPACT WISH:

“To finally have a way of preventing and treating diseases that each year afflict large populations, young and old, as well as having an effective means of stopping the next pandemic in its tracks.”

WAYNE I. LENCER, MD

Professor of Pediatrics
Harvard Medical School
Chief, Division of Gastroenterology,
Hepatology and Nutrition
Harry Schwachman Chair in
Pediatric Gastroenterology
Boston Children's Hospital



LESSONS LEARNED

FROM CHOLERA

FOCUS: *Developing an oral application for a therapeutic peptide that normally has to be given by injection.*

To safeguard against the world, our bodies have barriers that only small molecules like single sugars or single amino acids are able to cross into our gastrointestinal tract, lungs and sinuses, for example. But over time, some microbes have learned how to exploit pathways that get past these barriers, enter our bloodstream and cause disease.

“In studying the cholera toxin, we saw that it breaches the barrier by binding to a particular lipid,” Dr. Lencer says. “We found that we could fuse a peptide to a lipid that we engineered, and this fusion could cross the cell into the bloodstream.” The ability to deliver drugs in this novel way to normally impossible to reach tissues would be a real breakthrough, as small therapeutic peptides can treat diabetes, infertility and obesity, and therapeutic proteins have been applied to many inflammatory diseases and cancer.

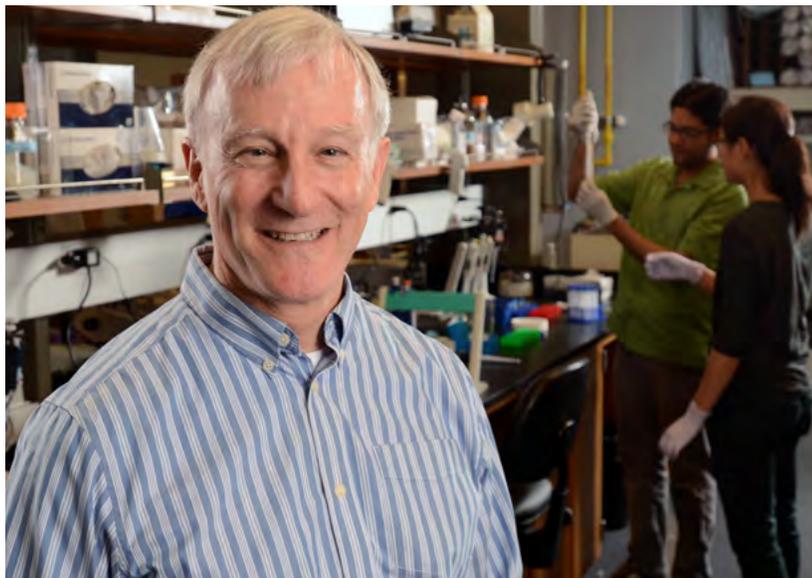
“In addition to the GI tract, lungs and bloodstream, our platform may work to cross the blood brain barrier—that would be another significant achievement, as getting antibiotics into the brain from the bloodstream isn’t easy,” Dr. Lencer says.

“Harrington is helping us organize the studies, to streamline the chemistry, and they’re assisting us with the commercial application,” Dr. Lencer says. “There I was, simply trying to cure cholera, and now we have an incredible team of experts with a chance at making a huge contribution to clinical medicine.”

IMPACT WISH:

“To develop an easier way to deliver therapies to the lungs, GI tract, heart, muscles and brain, is one of the holy grails of medicine.”

NEW HOPE FOR TREATING CHRONIC PAIN



IMPACT WISH:

“How wonderful it would be to have a safe drug for chronic pain that doesn’t lead to addiction, as well as a long-term drug that’s safer than acetaminophen or ibuprofen.”

ROBERT O. MESSING, MD

Professor of Neurology
Dell Medical School
Director, Waggoner Center for
Alcohol and Addiction Research
University of Texas at Austin

FOCUS: *Developing a safe, non-addictive drug for people with chronic pain.*

As one who in youth experienced the impact of alcoholism within his family, perhaps it’s no surprise that Dr. Messing’s journey as a neuroscientist led to a desire to understand how cells withstand and adapt, biochemically, to living in an alcohol environment. This work led to the discovery that in mice, the enzyme protein kinase C epsilon (PKCε) promotes alcohol consumption.

This finding piqued the interest of colleague Jon Levine MD, PhD, and together they

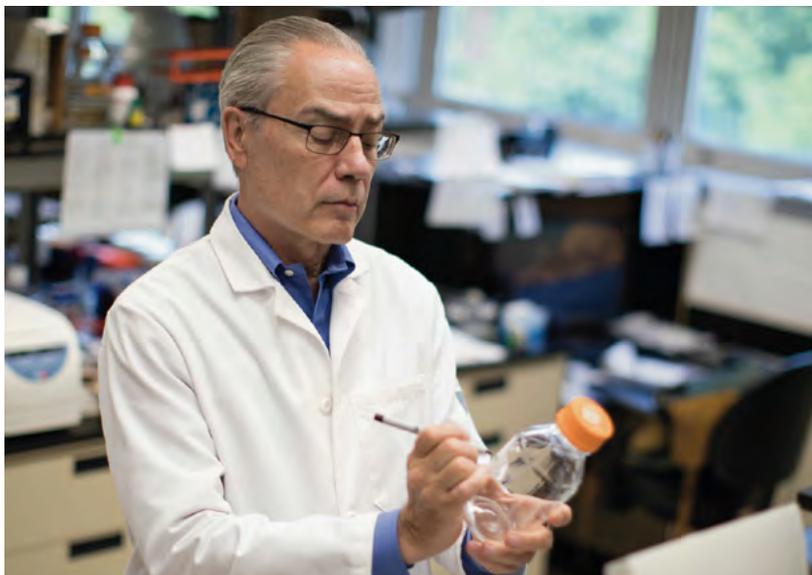
discovered that (in animal models) PKCε mediates pain provoked by alcohol, cancer chemotherapeutic agents, diabetes, stress and inflammation. Their work led to the discovery of a potent small molecule inhibitor of PKCε that reduces pain in animals.

Working with Stan McHardy, PhD at University of Texas at San Antonio, and Peter Bernstein, PhD and others within the Harrington Discovery Institute, they are focusing on optimizing the inhibitor

and pinpointing the best pain indication for testing.

“The drugs we have for pain are either addictive (opioids), or have side effects that prevent them from being used for extended periods,” Dr. Messing says. “So, as you’d expect there is a lot of drug company interest in developing compounds such as ours.”



**VICTOR L. SCHUSTER, MD**

Senior Vice Dean
 Professor, Department of Medicine and
 Department of Physiology and Biophysics
 Ted and Florence Baumritter Chair in Medicine
 Albert Einstein College of Medicine

A HEALTH ISSUE

WEIGHING ON AMERICA

FOCUS: *To develop a drug to mitigate and reverse nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) in patients.*

With one-third of Americans obese, nonalcoholic fatty liver disease has become the country's most commonly diagnosed liver problem. "The obesity epidemic isn't being mitigated by dieting or the five FDA-approved obesity drugs," Dr. Schuster says. "So it's no surprise that scientists have been searching for drugs that could prevent fat from accumulating in the liver."

In 1995, Dr. Schuster discovered what he dubbed the prostaglandin transporter (PGT), a protein that regulates the uptake and metabolic clearance of certain lipids in tissues throughout the body.

Years later, his team found that mice could live without the PGT gene, and had one-third the body fat of normal mice, even while consuming twice as much food. "These mice were very lean, with low body fat... they would be the envy of other mice at the beach," Dr. Schuster says.

"If we can find a drug that blocks PGT in people, we will have a safe way to treat NAFLD."

An anti-PGT compound was developed—the only potential NAFLD drug in the known research pipeline that targets PGT. Dr. Schuster and his colleagues are now testing the safety and efficacy of this compound and related molecules in work supported by the Harrington Discovery Institute.

IMPACT WISH:

"By providing novel and effective treatment for NAFLD/NASH, the medical impact of PGT inhibition would be vast, along with the potential to help reverse the widespread and relatively recent trend toward obesity."

GREAT STRIDES TO **AVOID SURGERY**

EACH YEAR APPROXIMATELY
350,000
INDIVIDUALS WORLDWIDE DIE
FROM HEAD AND NECK CANCERS

FOCUS: *Developing an anti-tumor drug for cancers originating in the lung, head and neck, and esophagus.*

For a scientist/surgeon, how validating would it be to see your long and dedicated research result in curing the very patients who would otherwise end up on your operating table? This may be the case one day for Dr. Singh, who each year performs 300–350 surgeries pertaining to head and neck cancers.

Squamous cell carcinomas of mucosal origin (mSCCs) include cancers originating in the lining of the lung, head and neck, and esophagus, and account for about one-fifth of all cancers worldwide.

Fifteen years ago Dr. Singh was identifying prognostic markers, work which ultimately led to his discovery of a novel gene, SCCRO (AKA DCUN1D1) that was involved in the development of these cancers. He spent years experimenting to understand how it functions, as pinpointing mSCC cancers is more difficult than, say, melanoma, where there are mutations in genes that are fairly common and can be targeted.

Dr. Singh's team has developed a promising compound that is able to inhibit activity in the SCCRO protein, and with support from Harrington Discovery Institute are optimizing it to prepare it for use in humans.



BHUVANESH SINGH, MD, PHD, FACS

Director, Laboratory of Epithelial Cancer Biology
Co-Director, Multidisciplinary Skin Cancer
Management Program
Memorial Sloan Kettering Cancer Center

IMPACT WISH:

“It would be such a large step forward if we were able to improve responses to cancers of the head, neck and lung, and skin cancers like melanoma.”

DAVID B. SYKES, MD, PhD
Assistant Professor of Medicine
Massachusetts General Hospital
Center for Regenerative Medicine
Harvard Medical School



TRICKERY AT **THE CELLULAR LEVEL**

FOCUS: *To identify new and unexpected therapeutic targets for the treatment of acute myeloid leukemia (AML).*

Albert Einstein said, “The most beautiful thing we can experience is the mysterious. It is the source of all true art and science.” Dr. Sykes is indeed working with a beautiful mystery. He has found a way to trick leukemia cells into maturation by inhibiting the enzyme dihydroorotate dehydrogenase (DHODH) within those cells. The reason this occurs is not clear, but the implication certainly is: people with AML could receive a treatment dramatically superior to what has been a mostly unmodified standard of care for more than four decades.

“Any interruption in the balance of cells being created and cells dying leads to an accumulation of immature cells that no longer respect that normal process,” Dr. Sykes says. “Cancer cells are not inherently malicious—they are simply confused, stuck in an immature state. Traditionally we have killed immature cells with chemotherapy, with its expected side effects. With help from Harrington we are building upon this foundation of differentiation therapies to find targets beyond DHODH that will set those cells back into the normal process of development.”

“This work is focused on AML, but we are also exploring how the concept of differentiation therapy and how these molecules in particular might be able to address other cancers, and in particular other solid tumor malignancies,” Dr. Sykes says.



IMPACT WISH:

“Imagine a well-tolerated drug that spares normal cells while specifically promoting the maturation of leukemia cells. In other words, imagine a superior alternative to chemotherapy.”

POTENTIAL BREAKTHROUGH FOR BUILDING BONE

FOCUS: *Creating a new therapeutic for osteoporosis.*

If you were to write a movie about a doctor who became dedicated to preventing osteoporosis, it's likely that your script would follow a progression similar to Dr. Wein's career. As a grad student he became interested in bone biology, getting his PhD in immunology. After med school, as an endocrinologist Dr. Wein began treating many patients with osteoporosis, and before long realized that current treatments weren't the answer.

"Most current treatments slow the rate at which bone tissue breaks down," Dr. Wein says. "One drug, parathyroid hormone (PTH), forms new bone, but must be injected daily.

That's a major downside, as most people simply won't inject every day for a condition that has no apparent symptoms."

In the lab he noted that the actions of PTH in bone involve a signaling cascade that turns off salt inducible kinases (SIKs).

After several years of research, Dr. Wein's team, with help from collaborators at the Dana-Farber Cancer Institute and the Broad Institute, found that a small molecule SIK inhibitor, YKL-05-099, builds new bone by mimicking the effects of parathyroid hormone. They also found that, in mice, this inhibitor reduced levels of the cells

responsible for bone breakdown—meaning that small molecule SIK inhibitors could potentially stimulate bone formation and suppress bone resorption.

"As common as osteoporosis is, with help from the Harrington Discovery Institute, we may be able to turn this new knowledge into a blockbuster drug that would help millions," Dr. Wein says.



FOR MORE INFORMATION, PLEASE VISIT:
harringtondiscovery.org/Videos



IMPACT WISH:

"By 2033 there will be more Americans over 65 than under 18. I hope that well before then, simply by taking a pill, older people will be able to avoid broken bones, staying more whole, healthy and active."

MARC N. WEIN, MD, PhD

Assistant Professor of Medicine
Massachusetts General Hospital
Harvard Medical School



ADRIAN WIESTNER, MD, PhD
Senior Investigator
Laboratory of Lymphoid Malignancies
National Heart Lung and Blood Institute
National Institutes of Health

NO ESCAPE FOR TUMOR CELLS

FOCUS: *Developing new and better therapeutics to treat hematological malignancies.*

One of the biggest roadblocks in fighting cancer is the ability of tumors to adapt in such a way as to escape our current treatments.

“We don’t fully understand what happens inside the cancer cells when they are hit by the treatments we use in our patients,” Dr. Wiestner says. “Specifically, we ask what stress is the treatment triggering in the cancer cells, and why are some cells able to resist?”

Dr. Wiestner and his team have developed experimental antibodies that, when combined with an existing FDA-approved therapeutic antibody, effectively attack cancer cells, including those cancer cells that have found ways to evade being killed by conventional monoclonal antibodies.

“My father had Hodgkins lymphoma in the 1970s...he was lucky in the sense that by then people had figured out chemotherapy and were able to cure it,” Dr. Wiestner says.

“I hope that the work we’re doing will lead to many more patients and their families feeling they were fortunate to live in a time when there were solutions to their cancers.”

As his team strives to move from preclinical models to human trial, Dr. Wiestner acknowledges the support from the Harrington Discovery Institute’s Therapeutics Development team.

“The Harrington folks are showing me how to get out of my physician-scientist shoes and into entrepreneurial shoes.”

IMPACT WISH:

“We may have discovered a general principle by which antibody therapy can be made more effective so that it will benefit many patients with lymphoma, leukemia, multiple myeloma, and perhaps even solid tumors, such as colon and breast cancer.”

TWO BREAKTHROUGHS FOR **THE PRICE OF ONE**

FOCUS: *To develop an antibody that reduces bone loss and body fat.*

There are estimated to be 108 million obese children and 604 million obese adults worldwide. It is humankind's most pervasive health problem.

Osteoporosis is estimated to be a major public health threat for tens of millions of American women and men aged 50 and older. What if a drug was developed that was capable of reducing both osteoporosis and obesity?

Although such a drug may be a few years from being a reality, the story of Dr. Zaidi's work made its way to the New York Times, as well as prestigious journals like The New England Journal of Medicine and Cell Metabolism and was selected by Nature Medicine as one of the top eight Notable Advances in biomedicine for 2017.

"In studying how the follicle-stimulating hormone (FSH) affects bone mass, we found that it is also tied to a characteristic redistribution of weight to the abdomen," Dr. Zaidi says. "In mouse studies

we found that blocking the hormone not only increased bone mass, but increased the calories burned, reduced body fat, and even encouraged physical activity."

With support and guidance from the Harrington Discovery Institute, Dr. Zaidi will be studying the efficacy and safety of monoclonal antibodies designed to block FSH, which show remarkable promise in animal studies.

The most obvious target audience is post-menopausal women who typically lose bone mass and gain weight—yet the implications are potentially vastly broader, for men as well.



FOR MORE INFORMATION, PLEASE VISIT:
harringtondiscovery.org/Videos



MONE ZAIDI, MD, PhD

Director, The Mount Sinai Bone Program
Professor of Medicine, Endocrinology
Diabetes and Bone Disease
Icahn School of Medicine at Mount Sinai

IMPACT WISH:

"Imagine a single agent capable of mitigating or preventing not one, but two of the most ubiquitous conditions the world over: obesity and osteoporosis."

DIANNE M. PEREZ, PhD

Professor and Staff
Department of Molecular Cardiology
Cleveland Clinic Lerner Research Institute



HALFWAY TO A MIRACLE

FOCUS: *To design a drug capable of halting, reversing or preventing Alzheimer’s disease (AD).*

One day in 2011, after working for 21 years on therapeutics for vascular diseases, Dr. Perez made a surprising discovery in the lab. The next day her career became about Alzheimer’s disease.

The remarkable discovery was that a compound she was developing to protect against cardiac ischemia turned out to offer significant benefits on cognition, learning and memory in mice.

“We were working with α 1-adrenergic receptor agonists, which cause blood vessels to narrow, increasing the chances of stroke or heart failure,” Dr. Perez says.

“But once we saw the other benefits, we realized we had found a mechanism never before explored in the Alzheimer’s disease field. The task became designing a smarter drug that could uncouple the cognitive benefits from the potentially harmful effects on blood pressure.”

Dr. Perez and her team synthesized one particular compound—dubbed “Compound 3”—which did just that. With the initial support of the BrightFocus Foundation and subsequently the ADDF-Harrington Scholar award, Dr. Perez has begun testing the compound’s effects in a preclinical

model of AD. A preliminary study in mice has shown significant increases in learning and memory functions. A second, more in-depth study is now being designed.

Following this phase of the project, Dr. Perez plans to find ways to optimize Compound 3 (which is patented by Cleveland Clinic) before pursuing clinical trials in AD patients.

 FOR MORE INFORMATION, PLEASE VISIT: harringtondiscovery.org/Videos

 EVERY
65 SECONDS
SOMEONE IN THE U.S.
DEVELOPS ALZHEIMER’S DISEASE

IMPACT WISH:

“With AD becoming more rampant, to have a drug with the potential to help many millions of people, not just help with symptoms, but management of disease, perhaps even repairing neurons that are being lost.”

HOPE FOR A DEVASTATING DISEASE

FOCUS: *Developing a gene therapy that preserves or restores vision in patients with Usher Syndrome 1B.*

Broadly, the three types of Usher syndrome are characterized by partial or total hearing loss, as well as vision loss that worsens over time. With Type 1, individuals are born profoundly deaf, and experience progressive vision loss that begins in childhood. “This form of Ushers is especially heartbreaking, as just when the individual and their family has come to grips with their deafness, they learn that blindness is likely,” Dr. Boye says.

Usher syndrome is further subdivided into types, based on the mutated gene causing

the disease. Dr. Boye’s focus is on type 1B which is caused by mutations in the gene MYO7A. “The idea is to deliver a healthy copy of MYO7A to the retina of these patients,” Dr. Boye says. “But the vector currently being used to deliver genes to patient retinas isn’t big enough to accommodate a gene this large. We therefore split MYO7A in half, and deliver both halves to the retina via two different vectors. Gene halves are designed to have complementary sequences, which allows them to find each other, bind together, and form full length MYO7A.”

If successful, this dual vector method would change the game for other investigators seeking to address retinal diseases associated with mutations in large genes.

“I’ve long been fascinated with neuroscience, and the idea that we can use gene therapy to restore someone’s vision was very moving to me,” Dr. Boye says. “Nothing spoke to me more than the concept of helping a blind person to see again.”



IMPACT WISH:

“I want to restore/preserve people’s eyesight, enabling them to most effectively navigate their way through daily life.”

SHANNON E. BOYE, PhD

Associate Professor
Department of Ophthalmology
University of Florida College of Medicine

RICHARD H. KRAMER, PhD

Professor, Department of Molecular and Cell Biology
CH and Annie Li Chair of Molecular Biology of Diseases
University of California, Berkeley School of Optometry



LET THERE
BE LIGHT

FOCUS: *To make a drug formulation that restores vision to those afflicted with retinitis pigmentosa (RP) and other age-related degenerative blinding diseases.*

Dr. Kramer has always been deeply gratified by attempting to unravel the mysteries of how the nervous system works. As with many of the Harrington Scholars, his boundless scientific curiosity and dedication eventually led him to devote a substantive percent of his research efforts toward a specific biomedical need.

Retinitis pigmentosa and age-related macular degeneration (AMD) are blinding diseases caused by degeneration of the light-sensing neurons in the retina. An

estimated 100,000 people in the U.S. have RP, mainly caused by inherited gene mutations. Most people with RP are legally blind by age 40.

As for AMD, one in ten octogenarians have some form of the disease, making it one of the leading causes of vision loss on the planet.

Using optopharmacology, where drugs are activated and deactivated with light, Dr. Kramer's team has found a way to

bestow light sensitivity onto the ordinarily light-insensitive retinal neurons of mice. The results of intraocular injection of BENAQ, their most promising photoswitch (a chemical sensitive to light), indicates reconstitution of light signaling through brain circuits.

"There is pure scientific joy when one makes a discovery," Dr. Kramer says. "But to know our work has the potential of helping restore people's ability to see has even doubled my enthusiasm for scientific research."

IMPACT WISH:

"Our work represents a critical step in the development of a simple drug treatment for restoring or improving visual function in human blinding diseases."

KEEPING CELLS ALIVE

FOCUS: *Identifying molecules that can prevent cell death and potentially treat a wide range of retinal degenerative diseases and other conditions.*

From a young age Dr. Matsuyama was fascinated by what is perhaps the most fundamental question in all of life science: why is there death? His pursuit of answers has guided his career path and is revealing insights into cell behavior that could one day have a significant impact on the human condition.

“Rice has a one-year lifespan, yet cedar trees have unlimited lifespans. The cells of mice and humans look nearly the same, yet humans live 25 times longer,” Dr. Matsuyama says. “I am fascinated by evolutionary theory, how lifespans are controlled. One practical way to study that mechanism was to understand programmed cell death, and in turn to try and invent technology to prevent it.”

BAX (BCL2-Associated X Protein) and BAK (Bcl-2 homologous antagonist killer) are proteins that regulate mitochondria to control the death and survival of cells.

With support and funding from the Gund-Harrington award, Dr. Matsuyama’s team is developing clinically-effective small compounds that inhibit BAX and BAK in order to protect retinal cells from death.

If successful, his drug could be applicable to many forms of retinal disease, independent of the underlying genetic mutation. In addition, these new cell-death inhibitors are expected to protect other cell types in the body, including neuron and hematopoietic stem cells.



SHIGEMI MATSUYAMA, PhD, DVM

Associate Professor of Medicine
Department of Pharmacology
Case Western Reserve University

IMPACT WISH:

“Our aim is to develop compounds that can prevent degenerative retinal diseases and ultimately, some causes of blindness. There is even potential for this technology to reduce the number of deaths or catastrophic effects of a range of pathological conditions, such as stroke, infections, traumatic injuries, and others.”

CONVERTING RODS TO CONES: **SEEING IS BELIEVING**

FOCUS: *Developing a treatment to prevent blindness and compromised sight in patients with retinitis pigmentosa (RP).*

Dr. Reh's years of dedicated work on retinal regeneration started with his fascination at how amphibians regenerate eyes and limbs. But stimulating the regeneration process in patients with retinal disease is still some years off, and now he and his team may have found a faster way to help patients with retinitis pigmentosa.

RP is a group of rare genetic disorders that involve a breakdown and loss of cells in the retina, with vision worsening until usually only a small area of central vision

remains—akin to looking through a straw. Often all vision is eventually lost.

Studies of the developing retina showed that the rods and the cones originate from the same progenitor, but a molecular switch, called NR2E3, makes the cells become rods. "Since RP starts in the rods, we thought that if we could convert the rods to cones, the newly formed rod-cone hybrid cells might not die from the disease," Dr. Reh says. "So we looked for drugs that could inhibit the function of NR2E3, and

discovered a small molecule we dubbed Photoregulin3 that seems to work."

In mice, Photoregulin3 partly converted the rods to a more cone-like state, and sure enough this stopped them from degenerating. Funding from the Harrington Discovery Institute allowed Dr. Reh's team to acquire the key data to start a biotech company, whose aim is to make the molecule more potent, and if possible, adapted to work as a pill.

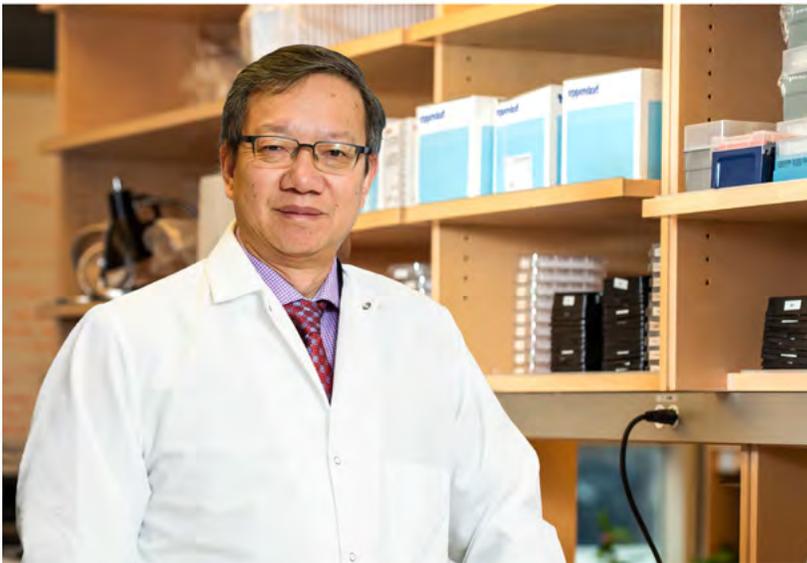
THOMAS REH, PhD
Professor of Biological Structure
University of Washington School of Medicine



AN ESTIMATED
100,000
PEOPLE IN THE U.S. HAVE
RETINITIS PIGMENTOSA

IMPACT WISH:

"With a pill taken perhaps once a week, people with RP will retain their eyesight throughout their lives."

**ZHENG-RONG LU, PhD**

Professor, Department of Biomedical Engineering and Department of Radiology
Case Western Reserve University
School of Medicine

IMPACT WISH:

“To preserve the vision of kids with Stargardt disease, easing the burden that blindness is to the individual, their family, and society.”

A RARE APPROACH TO A RARE DISEASE

FOCUS: *Developing a non-viral gene therapy for Stargardt disease, the most common form of inherited juvenile macular degeneration.*

As with most of the scientists profiled in these pages, the work for which Dr. Lu received his Gund-Harrington award didn't stem from a particular career goal. It is often a mix of driven scientific curiosity, specific areas of expertise, and happenstance. “I've always aimed to figure out better ways to help people suffering from all kinds of diseases, pure and simple,” Dr. Lu says. “My work investigating novel drug delivery therapies, nanomedicine, biomaterials, etc. has led me to Stargardt disease.”

Usually appearing in childhood or adolescence, almost everyone with Stargardt has extremely poor visual

acuity, in the range of 20/200 to 20/400, and it is not correctable with prescription eyeglasses or refractive surgery.

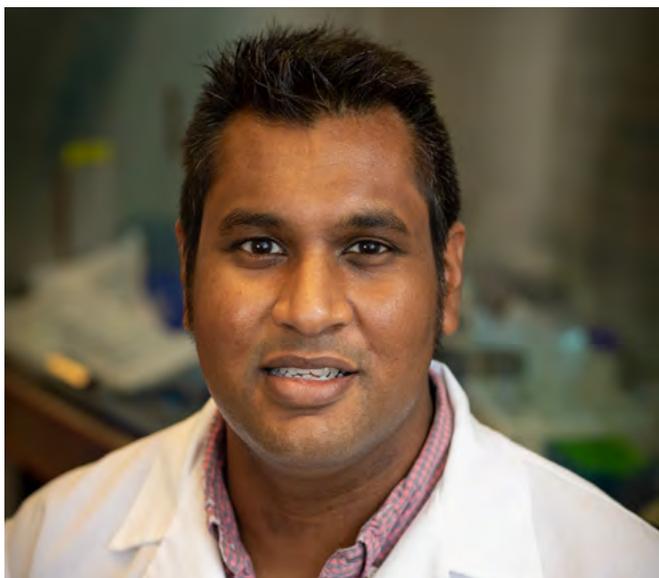
Gene therapy, where genetic material is introduced into cells, is a promising approach to diseases which, like Stargardt, are caused by a mutation in a single gene. However, the Stargardt gene is too large for current gene therapy techniques to correct the mutation.

“We have designed a non-viral system using novel lipid DNA nanoparticles,” Dr. Lu says. “In a mouse model of Stargardt, the nanoparticles have demonstrated the safety and efficacy

necessary for delivering the large therapeutic gene to the retina, in turn slowing down the progression of the disease.”

With help from the Harrington Discovery Institute, the goal is to optimize the nanoparticles for clinical translation, perform safety studies required by the FDA, eventually running clinical trials in patients.

Learn more about Dr. Lu's work on page 36.



KRISHANU SAHA, PhD

Assistant Professor
Department of Biomedical Engineering
University of Wisconsin-Madison

IMPACT WISH:

“We hope to improve vision for patients afflicted by inherited genetic disorders, with low potential for adverse events; and that this work will be a springboard to further discoveries in genomic medicine.”

THE EYES ARE THE

WINDOW TO BREAKTHROUGHS

FOCUS: *Developing gene-editing therapies that can help or cure a far greater number of people whose sight is afflicted by inherited genetic disorders.*

“The most exciting part of my work is to meet my former trainees and hear about their successes,” Dr. Saha says. “I’m always impressed by how much my trainees accomplish after they leave my lab.”

Considering the breakthrough work going on in that lab, no doubt his trainees depart with a sense that they can achieve most anything.

Dr. Saha’s work is aimed at genetic disorders that afflict the retinal pigment epithelium (RPE), the cell layer just outside the neurosensory retina. Its many functions include light absorption, supplying nutrients to photoreceptors, converting light to electrical signals, and removing pathogens and cell debris.

These disorders, such as some forms of retinitis pigmentosa, Best disease and congenital amaurosis, all greatly hinder eyesight, some leading to blindness.

The usual current therapy, the viral treatment of delivering lab-formed DNA molecules into the cells, has limitations, and some patients’ gene makeup isn’t suited for this approach.

Dr. Saha and his team are working on generating nanocarriers of gene-editing machinery that sidestep the safety issues of viral delivery. “Advancements have enabled precision gene-editing directly in patient tissues,” Dr. Saha says.

“But beyond helping disorders that affect the eyes, our approach could set the foundation for a new paradigm in genomic medicine, expanding the types of tissues that could be edited, and hence the spectrum of disease where genomic medicine could have an impact.”

BRIDGING THE GAP

Harrington Discovery Institute provides funding and expert resources that provide a high level of technical and commercial support to all Harrington Scholars.

WHERE GENIUS AND DEDICATION MEET EXPERIENCE



DIANA R. WETMORE, PhD
 Vice President
 Therapeutics Development
 Harrington Discovery Institute

Since every scientist applying to be a Harrington Scholar-Innovator is doing potentially breakthrough drug discovery work of some kind, extensive evaluation is necessary before selection decisions are made.

An initial review of the applications is conducted by Harrington Discovery Institute leadership to assess responsiveness to the program call. The applications are then evaluated by academic science reviewers and pharma/industry reviewers who look at the applications from multiple perspectives. This evaluation stage involves an Executive Committee comprised of physicians and research scientists. The third and final review is conducted by the Harrington Discovery Institute Scientific Advisory Board who ultimately select the most promising projects to receive the Scholar-Innovator grant.

“Before a scholar gets the grant, we look at the science, we analyze the markets relevant to the work, we look for any red flags related to the intellectual property,” says Diana Wetmore, PhD, Vice President of Therapeutics Development, Harrington Discovery Institute.

“We typically award scientists whose work is in the pre-clinical phase,” says Project Manager Troy Gobbett. “If their work is too early, we can’t be of as much help because we’re more about translating and helping to accelerate and optimize what they’ve already discovered. They have to have a prototype, not just an idea.”

Usually it takes a few months between a scholar’s application and the initial project kickoff meeting, when team members travel to the scholar’s institution and meet for a few hours to discuss the science involved.

“Our Therapeutics Development team will conduct a deep dive assessment into the scholar’s project,” says Michael Hallen, Project Manager Associate. “We use a templated evaluation of various criteria on the scholar’s application, as well as what we might find publicly in scientific journals, etc.”

“We don’t own these projects,” explains Dr. Wetmore. “It’s the scientist’s work, and it’s our job to persuade her or him that our advice can be trusted.

Fortunately, as the Harrington Discovery Institute is becoming more and more renowned, with each passing year that’s getting easier to do!”

Aside from the deeply gratifying work of shepherding breakthrough therapies toward commercialization, the breadth of disease conditions being addressed by the 110 Harrington scholars makes being a drug development advisor a fascinating job. “In the past, I was always in a single lane—I worked only on ALS or MS. Here, it’s such a diverse portfolio, every day offers an entirely new challenge of some sort,” says Project Manager Simon Mazza-Lunn.

“Like these scientists, our goal is to help humankind,” Dr. Wetmore says. “And our advisors are eager to share the knowledge that took them a lifetime to gain.”

**SIEW HO, PhD**

Strategic Advisor
Harrington Discovery Institute

MICHAEL AHLJIAN, PhD

Strategic Advisor
Harrington Discovery Institute

AN ALL-STAR ADVISORY TEAM

Traditionally in academia, if you publish in high-profile journals with some frequency, you're going to have a successful career. But what a scientist needs in order to generate a paper is different from what he or she needs to develop a potentially therapeutic molecule that could ultimately benefit patients.

Enter the Strategic Advisors from Harrington Discovery Institute's Therapeutics Development team. These advisors are deeply experienced professionals offering specialty skills in key scientific and/or therapeutic areas, serving our Harrington Scholars either as lead advisors or on an ad hoc basis.

One Strategic Advisor, Michael Ahljian, PhD, provides deep expertise in neuroscience. He has had success in discovering molecules in the lab to test in humans, and helping to design and interpret clinical studies. Most of this effort has been in neurology-related indications, especially Alzheimer's disease and Parkinson's disease. He has also worked in neuromuscular diseases, such as ALS (Lou Gehrig's disease) and Duchenne's Muscular Dystrophy.

"The academic scholars we work with represent a wide continuum of knowledge about therapeutics," Dr. Ahljian says. "As data regarding a potential therapeutic approach emerge from their laboratories, we help them define a critical path toward a therapeutic molecule. For those with no experience, we try to ground them in basic principles of drug discovery, and help them refine their experiments to increase the probability that at the end of the funding period they will be close to a molecule that could be tested in the clinic."

Another Strategic Advisor, Siew Ho, PhD, has extensive experience in nucleic acids research in the cardiovascular, metabolic diseases, neuroscience and virology areas. "Whereas small molecules and protein biologics are more traditional drug molecules, nucleic acid drugs, made from the same building blocks that comprise our genes, are an emerging therapeutic modality," Dr. Ho says. "Four nucleic acid drugs have been approved by the FDA in the last two and a half years. It's an exciting time to be doing research in this area."

"Few researchers are familiar with the intricacies and pitfalls associated with the development of this new class of molecules as drugs," she says. "That's where we can be of help to the Harrington Scholars."

"Sometimes when I explain to others who don't know what the Therapeutics Development team does," says Dr. Ho, "I detect a tone of amazement and 'that's incredible!'"

COLLABORATION DOWN TO A SCIENCE



KAUSHIK DAVE, PhD, MBA
Strategic Advisor
Harrington Discovery Institute

ZHENG-RONG LU, PhD
2018 Gund-Harrington Scholar

In the world of drug development, failure is circumvented by a thousand innovative twists and turns in the lab; but if a compound ultimately fails it's rarely a surprise. Only about one in every 5,000 compounds in preclinical development becomes an approved drug.

The fact that these people persevere in the face of such long odds is a testament to their dedication to doing something good and important for humanity.

The Harrington Discovery Institute is too young for there to be metrics proving our ability to make those odds any less overwhelming, but considering the invaluable input our Therapeutics Development team brings to the work of our scholars, the formula is surely fostering a more successful drug development process.

Kaushik Dave, PhD, MBA, serves as a Strategic Advisor specializing in regulatory

and pharmaceutical development strategy and planning, guiding early discoveries toward investigational and marketing success. This work involves assisting Harrington Scholars as they try to take their idea, hypothesis, or very early-stage program into the clinic.

One of the projects Dr. Dave helped advance in 2018 was that of Gund-Harrington Scholar Zheng-Rong Lu, PhD, in his work to develop non-viral gene therapy for Stargardt disease, the most common form of inherited juvenile macular degeneration. (See page 31)

"Kaushik has been really helpful for us, beginning with a plan he created for the translation of development of our technology," Dr. Lu says. "Clinical translation for any therapeutic is a complicated process; I explained how the technology worked, and what kind of formulation we had in mind. Kaushik helped us design the formulation, and

"Clinical translation for any therapeutic is a complicated process; I explained how the technology worked, and what kind of formulation we had in mind. Kaushik helped us design the formulation, and advised us on the FDA-approved ingredients needed to make it stable, to control its physical properties. He has more practical knowledge than I have!"
says Zheng-Rong Lu, PhD.

advised us on the FDA-approved ingredients needed to make it stable, to control its physical properties. He has more practical knowledge than I have!"

Dr. Dave and Dr. Lu have regular phone calls, and meet every few months or so. Dr. Dave looks over all the new data that's been generated, and designs studies to assess whether what Dr. Lu and his team are doing is still relevant in light of the new information, suggesting tweaks if necessary.

With the abundant time and financial investment required for drug development, it's no wonder a common maxim in this field is "If you're going to fail, fail fast and soon, so you can try something else." Fail or succeed, Harrington Strategic Advisors like Dr. Dave are here to support the scientists every step of the way.



RAHUL ARAS, PhD
Strategic Advisor
Harrington Discovery Institute

BERNARD CAMBOU, PhD
Strategic Advisor
Harrington Discovery Institute

THE EXPERTISE AND DIPLOMACY OF DRUG DEVELOPMENT

When one of the Harrington Scholars has a product deemed ready for partnering, the Harrington Discovery Institute Exit team of advisors helps by drawing upon their deep experience in pharmaceutical business development, investment, and startups. There are partnering strategies to be developed, potential investors and/or partners to be identified, perhaps a company to be created.

One might think developing a drug would be solely about the efficacy, safety, and potential market for it, but the partnering process can be a bit of a dance.

“You have to clearly and succinctly articulate the value proposition,” says Bernard Cambou, PhD, a Strategic Advisor with many years’ experience working on biological products, proteins, molecular antibodies, and gene and cell therapy.”

“These are driven, passionate scientists, and if you tell them it’ll be extremely difficult to cure, for example, heart failure, that only motivates them more,” says Rahul Aras, PhD.

“You don’t send emails to all the pharma companies in the world; you select those that operate in that space...but even then, you have to look at their portfolio. Do they have gaps? Lifecycle management issues? Synergistic activities? An established commercial conduit to the end-user?”

“I’m never pushy with pharma professionals. Perhaps at first they say no because they worked on a project that was somewhat similar to the scholar’s, and it failed. Plus, big pharma gets about a thousand proposals a year. It’s my job to make them feel comfortable with the scientific potential. You have to be credible, with a balance of optimism and confidence, keeping in mind that, from pharma’s perspective, 90% of drugs that get into clinic, fail.”

Sometimes diplomacy is needed with the scholars themselves. “These are driven, passionate scientists, and if you tell them it’ll be extremely difficult to cure, for example, heart failure, that only motivates them more,” says Rahul Aras, PhD, another Strategic Advisor and a biotechnology CEO with extensive experience in advancing early-stage life science technologies.

“Sometimes we say, ‘We know you’ve been working for years on this, but if you make this change, it’ll provide more credibility to potential investors and pharma—and you’ll still get there, but in two steps rather than one,’” Dr. Aras says. “That’s asking a lot—for a scientist to pivot and switch indications—but scholars that are open to that can grow tremendously.”



SHOBHA PARTHASARATHI, PhD

Vice President

Strategic Alliances and Business Development
Harrington Discovery Institute

PRIMED FOR SUCCESS

Brilliant they may be, but generally speaking, scientists aren't business people. At least for a majority, their expertise does not include identifying and securing partnerships to bridge their research across the translational threshold to commercialization.

That is just one of the many roles of the Business Development team at Harrington Discovery Institute.

"We bring business expertise to the scholars from the very start, providing whatever resources and help they may need," says Shobha Parthasarathi, PhD, Vice President, Strategic Alliances and Business Development, Harrington Discovery Institute. "We think through the business strategy, consider potential partners, and identify those who would be interested in this technology. Sometimes there's urgency involved—especially when competition is stiff in that market."

"Very few in academia are trained to commercialize a drug," says Dr. Parthasarathi. "To enable decision-making, we have an Investment Advisory Board that provides insight through the lens of venture investors. Our advisors are former executives from pharmaceutical companies and founders of startup companies who steer these technologies in the right direction. Ultimately, our combined efforts accelerate drug candidates on their way to the clinic."

"We keep up on industry trends," says Joe Barone, Business Development Manager. "We stay abreast of evolving technologies, the current environment in the life science community. We have direct engagement with technology transfer offices, so we understand the challenges these scientists face at universities. We help the researchers de-risk their technologies and make them more attractive for downstream investors."

The support provided by the Harrington Business Development team is comprehensive. "We coach the scientists on how to effectively pitch their technologies," says Julianne Roseman, Associate, Strategic Alliances and Business Development. "There is no question that the projects coming out of Harrington have a greater chance of success than those coming straight from a university."

TAUHID ALI, PhD
Vice President
Head of TAK-celerator
Takeda Pharmaceutical Company Limited



BREAKTHROUGHS WITHOUT BORDERS

Bridging the early translational phase of research in academia and developing a pharmaceutical quality candidate is still a challenge. The Harrington Discovery Institute and Takeda collaboration is a novel attempt to bridge this Valley of Death and accelerate therapies to rare disease patients.

In 2017 Harrington Discovery Institute and Takeda formed a collaboration with the aim of removing barriers between the academic community and pharmaceutical industry, and to advance highly promising drug discovery and early stage development of rare disease programs through the Harrington Rare Disease Scholar Program, sponsored by Takeda.

“We found the model to be very intriguing. It goes beyond financial support and offers guidance to help physician-scientists

take their early concepts across that translational Valley of Death,” says Tauhid Ali, PhD, Vice President, Head of the Takeda TAK-celerator. This collaboration is another example of how Takeda is focused on fostering partnerships between academia and industry and its increasing commitment to the development of medicines in rare diseases.

“I love the vision that Dr. Stamler has for Harrington Discovery Institute—to deliver these transformative therapies to patients. We are perfectly aligned in that philosophy,” Dr. Ali says. With a rich rare diseases portfolio, he is eager to see how the complementary skill sets of the two organizations can quickly accelerate new ideas into therapies that can potentially treat patients.

“Takeda has built upon the competencies we have—our R&D model is externally focused toward identifying innovation, with a constant eye on how we can advance our pipeline,” Dr. Ali says. “We’re very proud of the fact that Harrington Discovery Institute has chosen to work with us, and we hope we can further extend and articulate this partnership at the next level.”

The collaboration is currently scheduled to end in March of 2020, and Dr. Ali says that the deadline creates a sense of urgency. “It keeps everyone honest because we need to hit those dates! Fingers crossed, we’ll achieve what we set out as a target.”

THE HARRINGTON PROJECT PATHWAY FOR A PROMISING DRUG



If one recurring theme in these pages stands out, it must certainly be acceleration. That is precisely what the Harrington Discovery Institute and BioMotiv, a mission-driven for-profit accelerator, were designed to do under The Harrington Project: accelerate breakthrough discoveries into medicines for the benefit of patients. Ideas that would otherwise probably languish, unfunded.

In early 2019, a drug developed in part by a 2016 Harrington Scholar-Innovator, Rama Mallampalli, MD, and by Bill Chen, PhD, was cleared by the FDA to begin a Phase I clinical testing. Indeed, KT-1002, is now nearing its first in-human trial.

This is the first approved IND (investigational new drug) application for a Harrington Scholar-Innovator project supported by BioMotiv. KT-1002 was developed for the treatment of a range of inflammatory conditions, including inflammatory bowel disease (IBD), which encompasses both ulcerative colitis and Crohn's Disease.

"This work began 12 years ago, beginning with four years in determining the protein target, the pathways involved in inflammation and how the biology works," says Dr. Chen. "Once we made sure the pathways were relevant, we designed a compound to target the protein. Then it took years to perform a great deal of research, assays and experiments to ensure that this

was the right molecule moving forward. You have to be very thorough, as the last thing you want is a molecule that fails in Phase III."

"Our project began with a focus on lung transplantation rejection," Dr. Mallampalli says. "However, with support from the Harrington Discovery Institute, we studied factors such as the market landscape, the unmet need in the drug pipeline, and FDA regulatory-specific pathways. This work led to a broader discovery and a novel platform for inhibiting inflammatory pathways, which in turn led us to focus on inflammatory bowel diseases such as Crohn's disease and ulcerative colitis."



KOUTIF THERAPEUTICS SCIENTIFIC FOUNDERS **BILL CHEN, PHD**, ASSOCIATE PROFESSOR OF MEDICINE, UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE AND **RAMA K. MALLAMPALLI, MD**, CHAIR, DEPARTMENT OF INTERNAL MEDICINE, THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE

“BioMotiv’s expertise in pharmacokinetics, regulatory and IND-enabling support propelled our technology, and we are excited to take our lead compound candidate to Phase I studies,” Dr. Mallampalli says.

In 2017, Koutif Therapeutics was formed as the biotechnology startup to develop this small molecule drug. “Koutif exemplifies how The Harrington Project vision was intended to work,” says Russ Wyborski, PhD, the BioMotiv Project Operations Director on Koutif. He has over 25 years of drug discovery and product development experience, much of that with big pharma companies.

“This setup simply doesn’t exist in big pharma,” Wyborski explains. “We are a small nucleus of people, not huge layers of management that you need to go through. In a large organization you have people at various levels of experience, which can be good; but our experiences are distilled down to the people needed to get a given drug to market—there is no dilution of responsibilities.”

Jeff Edelson, MD, BioMotiv’s Chief Medical Officer, agrees. “On each project, for whatever gaps our very experienced staff can’t fill, we assemble a team of best-of-breed consultants, advisors and vendors, customizing to meet the challenges of the

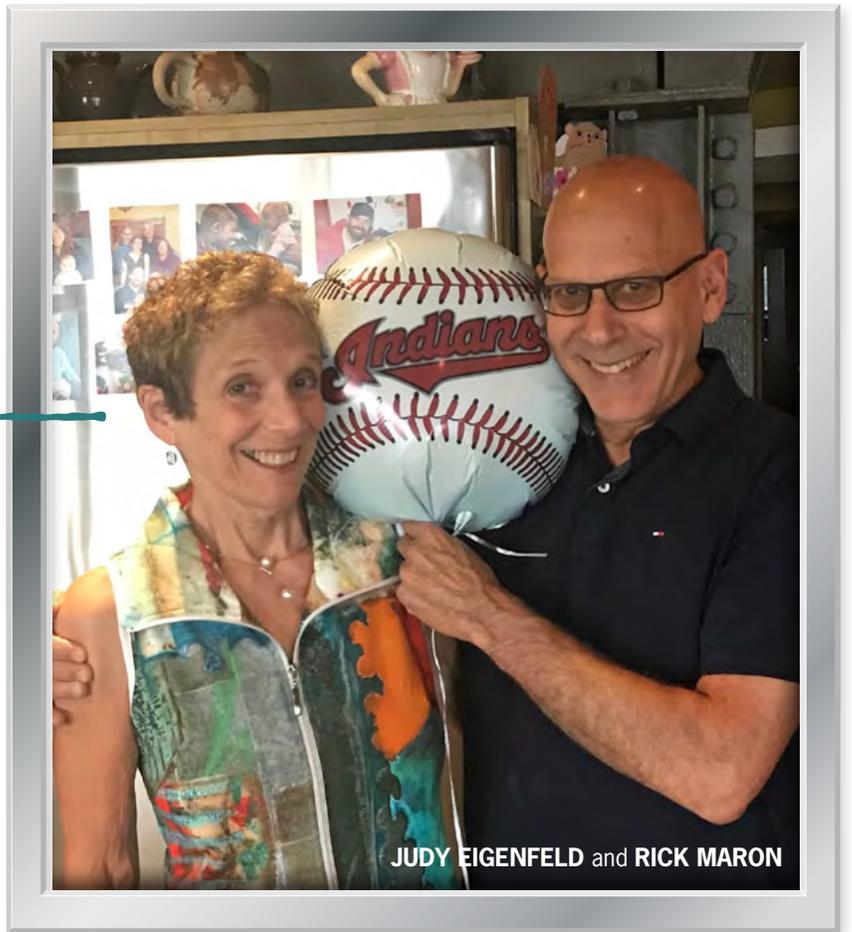
specific asset,” he says. Based on over 30 years in clinical development roles, he observed, “In big pharma, capital allocation can be quite inefficient, and a typical project’s workflow is unnecessarily long and complex. The BioMotiv model is much more agile, which serves our mission to move promising drugs through the pipeline more quickly.”

“Without support from BioMotiv we would’ve had significant challenges in fundraising and optimizing movement toward an FDA-approved product for human testing,” Dr. Mallampalli says. “Another huge factor is that the consultants with BioMotiv are very experienced and hence able to engage proactively and collaboratively with the FDA.”



TO LEARN MORE ABOUT BIOMOTIV, PLEASE VISIT:
biomotiv.com

A *fight*
TO REMEMBER



JUDY EIGENFELD and RICK MARON

OF THE TEN LEADING CAUSES OF DEATH IN THE U.S., ONLY ONE, ALZHEIMER'S DISEASE, CANNOT BE CURED, PREVENTED OR SLOWED.

Yet funding for research on Alzheimer's and related dementias is around \$1.4 billion, compared to \$6 billion for cancer and \$3 billion for AIDS. It's a tragic discrepancy, and the reason is obvious. Alzheimer's and dementia have always been seen as a natural aspect of the aging process.

That's changing. Fiscal year 2019 will see a historic \$425 million increase for Alzheimer's research at the National Institutes of Health.

But like the many millions who are suffering—the individuals who suffer from Alzheimer's, as well as their families and loved ones—Judy Eigenfeld and Rick Maron want answers far more quickly than are likely to result from the usual drug discovery process.

Judy was diagnosed with the disease in 2015. The couple's immediate reaction was to try and find a cure. "We thought, let's get involved, not just for Judy's sake, but for society's," Rick says.

"It has been a disease for 118 years, and in all that time, no way to deal with Alzheimer's has been found. There have been tremendous successes in vaccines, cancer, HIV, etc. Nothing for Alzheimer's."

The more research the couple did, the more committed they became. "Forty-seven million people have Alzheimer's. When you consider all the sufferers, including families and friends, there is nothing on earth with as devastating an impact on so many people," Rick says.

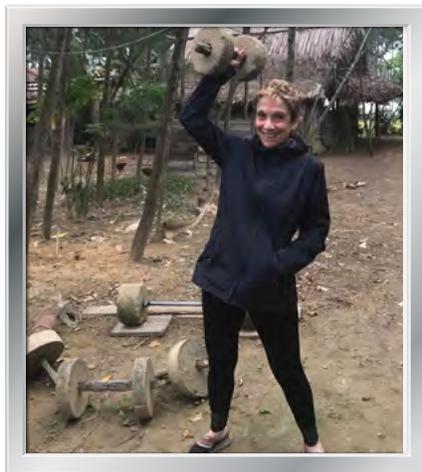
After a great deal of research, Judy and Rick landed on two organizations that they felt were the most likely keys to curing Alzheimer's. The first was Cure Alzheimer's Fund, a non-profit Massachusetts organization "dedicated to funding research with the highest probability of preventing, slowing or reversing Alzheimer's disease."

The other organization was the Harrington Discovery Institute.



“I fear for my kids, their kids. That is the essence of the need for a cure—to negate that genetic component.”

JUDY EIGENFELD



“The Harrington model made a lot of sense to us: committing funding to top scientists, helping them move the research along through the various phases,” Rick says. “We can support research, but if it’s just going to die on the vine, what’s the point?”

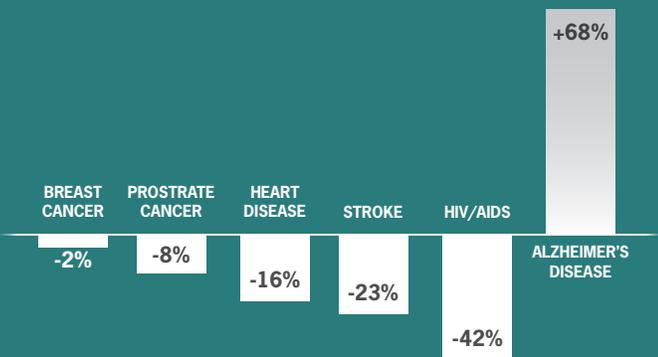
“What this disease needs more than anything is public awareness and public funding,” Judy says. “I feel good that we have identified two institutions that we feel are critical to this cause, and can do the most in coming up with a cure.”

“There’s a sense that maybe there is a future; maybe I won’t fail to recognize my own grandchildren or my sons, or my husband. To find a cure for Alzheimer’s, I will fight until I can’t fight.”

FACTS ABOUT ALZHEIMER’S DISEASE:

- 6th leading cause of death in the U.S.
- Worldwide, 50 million people are living with Alzheimer’s disease and other dementias
- 5.8 million Americans are living with Alzheimer’s
- By 2050, this number is projected to rise to nearly 14 million Americans
- Almost 2/3 of Americans with Alzheimer’s are women
- Early and accurate diagnosis could save up to \$7.9 trillion in medical and care costs

CHANGE IN DEATHS ATTRIBUTED TO MAJOR DISEASES FROM 2000–2010



SOURCE: alz.org/breakthroughACT

2018 SCIENTIFIC SYMPOSIUM



Jonathan S. Stamler, MD



John Crowley



Helen H. Hobbs, MD

CONVENING FACE TO FACE: VITAL TO THE MISSION

On May 23 and 24, 2018, global leaders in science, medicine and academia convened in Cleveland, Ohio for the Sixth Annual Harrington Scientific Symposium. Progress and growth were celebrated as new scholar classes were welcomed, including the 2018 Scholar-Innovators and 2018 Rare Disease Scholars, and scholars presented on the advances they had made in collaboration with their Therapeutics Development teams.

Harrington Discovery Institute President **Jonathan S. Stamler, MD**, talked about the importance of taking action. “For six years, we have been delivering innovative programs, developing powerful partnerships, launching industry-leading

products—all with a goal of benefiting patients in need,” Stamler said. Dr. Stamler provided an overview of the institute’s strategy and update on the initiatives that are advancing its mission.

Ronald G. Harrington, entrepreneur and philanthropist, shared his story as a grateful patient and expressed his family’s commitment to help those affected by diseases without cures. Mr. Harrington stressed that “grateful patients recognize that although they were successfully treated, many more people won’t be treated unless someone, some organization, or some ecosystem has enough heart, smarts, and resources to take action.”

Nunzio Bottini, MD, PhD, of UC San Diego, 2016 Scholar-Innovator, gave the Scholar Experience presentation, sharing his experience working with his Harrington project team to address next-generation therapies for rheumatoid arthritis. Dr. Bottini focused his message on the challenge of translating science into therapies. “Physician-scientists like me want to help patients through their science. But we are taught to discover, not translate. Harrington Discovery Institute is a creative and effective solution to the existing significant problem of translation from academia to industry.”

Keynote presenter **Christopher P. Austin, MD**, Director of NIH’s National Center for Advancing Translational Science (NCATS),



Ronald G. Harrington



“The conference is a physician-scientist’s wonderland. It was unique and invigorating to connect directly with individuals of such diverse and deep expertise, all motivated by a single purpose—to turn ideas into cures.”

SUNEET AGARWAL, MD, PhD
Boston Children’s Hospital
2018 Scholar-Innovator

reiterated the opportunity and need to deliver on the promise of science for patients. “It’s not that translation is new. It’s that the opportunity is far greater than it’s ever been. Therefore, the need to do this is far greater than it has ever been. And that’s going to require novel models for how to do this,” said Austin.

Some of the nation’s most accomplished medical innovators were in attendance, including Harrington Scientific Advisory Board members **David Ginsburg, MD, William G. Kaelin, Jr., MD, Andrew R. Marks, MD, Michael Welsh, MD,** and 2018 Harrington Prize recipient **Helen H. Hobbs, MD.** Dr. Hobbs received

the 2018 Harrington Prize for Innovation in Medicine for her discovery of the link between a gene mutation (PCSK9) and lower levels of LDL, or ‘bad cholesterol’, which is considered a major breakthrough and has improved the treatment of high cholesterol.

U.S. biotech executive and entrepreneur **John Crowley** gave an inspiring presentation about his personal experience raising funds and awareness to fight Pompe disease, a rare neuromuscular disorder affecting two of his children. The subject of a Hollywood film, *Extraordinary Measures*, Mr. Crowley told his story to illustrate the importance of Harrington Discovery

Institute’s work in translating scientific discoveries into medicines that advance the standard of care.

SAVE THE DATES:



MAY 20-21, 2020



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**2019 HARRINGTON
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MD, PHD**
University of Oklahoma

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Stanford University

GERALD W. DORN, II, MD
Washington University

JOACHIM HERZ, MD
UT Southwestern

PAUL W. HRUZ, MD, PHD
Washington University

PENG JI, MD, PHD
Northwestern University

V. VINOD MOOTHA, MD
UT Southwestern

DAWN M. WETZEL, MD, PHD
UT Southwestern

T.C. WU, MD, PHD
The Johns Hopkins University

ELLEN YEHL, MD, PHD
Stanford University

**2018 HARRINGTON
SCHOLAR-INNOVATORS**

SUNEET AGARWAL, MD, PhD
Boston Children's Hospital

JEFFREY S. GLENN, MD, PhD
Stanford University

WAYNE I. LENCER, MD
Boston Children's Hospital

ROBERT O. MESSING, MD
University of Texas at Austin

VICTOR L. SCHUSTER, MD
Albert Einstein College
of Medicine

BHUVANESH SINGH, MD, PhD
Memorial Sloan Kettering
Cancer Center

DAVID B. SYKES, MD, PhD
Massachusetts General Hospital

MARC N. WEIN, MD, PhD
Massachusetts General Hospital

ADRIAN WIESTNER, MD, PhD
NHLBI/NIH

MONE ZAIDI, MD, PhD
Icahn School of Medicine
at Mount Sinai

**2017 HARRINGTON
SCHOLAR-INNOVATORS**

PAUL L. BOLLYKY, MD, PhD
Stanford University

AMBROSE L. CHEUNG, MD
Geisel School of Medicine
at Dartmouth

GIULIO F. DRAETTA, MD, PhD
MD Anderson Cancer Center

SETH J. FIELD, MD, PhD
University of California,
San Diego

TODD D. GOULD, MD
University of Maryland
School of Medicine

JOHN J. LETTERIO, MD
Case Western Reserve University

DAVID B. LOMBARD, MD, PhD
University of Michigan

DARUKA MAHADEVAN, MD, PhD
University of Arizona

DEEPAK NIJHAWAN, MD, PhD
UT Southwestern Medical Center

STUART H. ORKIN, MD
Boston Children's Hospital

DANIEL S. ORY, MD
Washington University

**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. COLLER, 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
Boston Children's Hospital

RAHUL M. KOHLI, MD, PhD
University of Pennsylvania

IRINA PETRACHE, MD
Indiana University

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
Washington University
in St. Louis

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University of Pennsylvania

**GEOFFREY C. GURTNER,
MD, FACS**
Stanford University

RICHARD N. KITSIS, MD
Albert Einstein College of
Medicine

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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

2018 ADDF-HARRINGTON SCHOLAR

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Brigham & Women's Hospital

2017 ADDF-HARRINGTON SCHOLAR

DIANNE M. PEREZ, PhD
Cleveland Clinic
Lerner Research Institute

2016 ADDF-HARRINGTON SCHOLAR

TRAVIS L. DUNCKLEY, PhD
Arizona State University

SUNG OK YOON, PhD
The Ohio State University

2015 ADDF-HARRINGTON SCHOLARS

CAROL A. COLTON, PhD
Duke University

JERRI M. ROOK, PhD
Vanderbilt University

2014 ADDF-HARRINGTON SCHOLARS

THOTA GANESH, PhD
Emory University

CHIEN-LIANG LIN, PhD
The Ohio State University

2018 GUND-HARRINGTON SCHOLARS

ZHENG-RONG LU, PhD
Case Western Reserve University

KRISHANU SAHA, PhD
University of Wisconsin, Madison

2017 GUND-HARRINGTON SCHOLARS

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University of Florida

RICHARD H. KRAMER, PhD
University of California, Berkeley

SHIGEMI MATSUYAMA, PhD
Case Western Reserve University

THOMAS A. REH, PhD
University of Washington

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, FRCP**
University of Oxford

2015 OXFORD- HARRINGTON SCHOLARS

**HELEN MCSHANE,
MD, PhD, FRCP**
University of Oxford

**CLAUDIA MONACO,
MD, PhD, FESC**
University of Oxford

2014 OXFORD- HARRINGTON SCHOLAR

ALISON SIMMONS, MD, PhD
University of Oxford

IN MEMORIAM

GAVRIL W. PASTERNAK, MD, PhD
2014 Harrington Scholar-Innovator
Memorial Sloan Kettering
Cancer Center



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OUR MISSION:

To advance discoveries by physician-scientists, and all scientists in areas of unmet therapeutic need, into medicines for the benefit of society.