HARRINGTON DISCOVERY INSTITUTE MISSION:

To advance medicine and society by enabling inventive physician-scientists to turn their discoveries into medicines that improve human health.
HARRINGTON SCHOLARS
2012 – 2017

5 YEARS OF ADVANCING DISCOVERIES
The Harrington Project

Milestones Achieved - FIRST FIVE YEARS

In five years The Harrington Project has:

- Selected 5 classes of Harrington Scholars
- Supported 74 scientists
- Funded scientists at 41 institutions in the US and UK
- Launched 20 companies
- Open INDs
- Licensed 5 technologies to big pharma
Dear Colleagues,

In 2012 the Harrington family of Hudson, Ohio and University Hospitals made an important social-benefit statement with their creation of The Harrington Project for Discovery & Development and Harrington Discovery Institute. The Harrington Project established a unique model for drug discovery and development, pairing a non-profit institute, the Harrington Discovery Institute, with a mission-aligned, for-profit accelerator, BioMotiv. The eyes of investigators, investors and the pharmaceutical industry have increasingly focused on Cleveland, Ohio and this new model we designed to traverse the Valley of Death.

Five years later, we have much to be proud of. We have supported 74 Harrington Scholars who are advancing the standard of care globally. These scientists are both contributing important knowledge about some of mankind’s most serious diseases and making meaningful contributions toward treatments and cures. Their work shows great promise to advance standards of care in medicine.

Over the next five years, we will expand the Harrington platform to new therapeutic areas of unmet need. With this growth, you will see us increase our impact as we strive to realize our vision for a better world.

Thank you for your continued support of our mission. I’m proud of what we have accomplished together and enthusiastic about what lies ahead; I hope that as you review this annual publication, you’ll feel the same way.

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
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Harrington Scholars
Ronald G. Harrington Reflects on The Harrington Project’s First Five Years

As an entrepreneur, The Harrington Project for Discovery & Development co-founder Ronald G. Harrington thrives on challenges. When friends and associates told him five years ago the concept of The Harrington Project was “audacious and not likely to happen,” instead of discouraging him, their words strengthened his resolve.

Five years later, The Harrington Project has advanced the research of 67 physician-scientists (74 overall), progressed ten discoveries into clinical readiness, and established The Harrington Prize for Innovation in Medicine, helping to change culture in American medicine. Harrington is pleased but not surprised. After transforming his family business from near-obscurity to a market leader in the medical and surgical supply industry, Harrington knew his family would accept no less of this new endeavor. The quality of The Harrington Project leadership confirmed his “audacious” vision.

“I believe our success started on day one, when I met the people who would be part of this,” Harrington recalls. “We have the best of the best with Jonathan Stamler, Baiju Shah, Ted Torphy and David U’Prichard. Without people of this quality, the type of success we have had would never happen.”

Although the Harrington family launched the project through their generous gift of $50 million, to the family, it was never about a return on investment by conventional metrics. “We never looked at it that way,” Harrington says. “From the start this has been about the potential chance to find cures and improve people’s quality of life.”

The Harrington Project’s success in its first five years has bolstered the family’s resolve and dedication to its mission. Yet, with The Harrington Project as with business, Harrington is never satisfied with the status quo.

“We have great opportunities to make a difference right now,” he says. “In the next five years, I believe The Harrington Project will expand its global footprint and achieve results that substantiate our confidence in this unique drug development model we have created.”
The United States is a long-standing leader in biomedical research. In 2016, the National Institutes of Health (NIH) invested nearly $32 billion in medical research through some 50,000 grants supporting 300,000 researchers in 265 different diseases. Yet, in 2016 the United States Food and Drug Administration approved only 22 new drugs.* In 2004, then-NIH Director Elias Zerhouni, MD, dubbed this chasm between the laboratory bench and the clinic the "Valley of Death." In the 13 years since Dr. Zerhouni coined this phrase, major pharmaceutical companies and venture capitalists have withdrawn further from the metaphorical canyon's edge, unwilling to risk expensive dollars on advancing risky, still-unproven new drugs through the valley.

In 2012, the entrepreneurial and philanthropic Harrington family of Hudson, Ohio and University Hospitals created The Harrington Project for Discovery & Development. At its core, The Harrington Project was purpose-built to bridge the Valley of Death to bring life-saving, life-enhancing new medicines to the world.

Harrington Discovery Institute Chief Scientific Officer Mukesh K. Jain, MD, is committed to translating that promise into reality. "The Harrington Discovery Institute is well-positioned to impact the world by accelerating the development of new medicines that will advance standard of care and improve human health globally. In doing so, the Harrington Discovery Institute also helps University Hospitals fulfill its vision for a better world," says Dr. Jain who is also Chief Scientific Officer, University Hospitals Health System; Chief Research Officer, University Hospitals Harrington Heart & Vascular Institute; the Ellery Sedgwick Jr. Chair & Distinguished Scientist; and Vice Dean for Medical Sciences and Professor of Medicine, Case Western Reserve University School of Medicine.

“We have achieved two major milestones in the first five years,” he notes. “First, we established a new model for drug development, and second we have shown that the model works.”

It begins with Harrington Discovery Institute leadership’s identification of the best and brightest physician-scientists and scientists across the United States and in the United Kingdom through the Scholar-Innovator, Foundation and Oxford Scholar programs. "Then we support these investigators with both funding and a team of pharmaceutical industry experts tailored to each investigator’s needs through the Harrington Discovery Institute’s Innovation Support Center,” Dr. Jain explains. “The members of our Innovation Support Center constitute the ‘secret sauce’ that has made Harrington Discovery Institute so successful.”

Discoveries are advanced to pre-clinical milestones and/or through clinical “proof-of-concept” stages, and then transitioned to strategic partners for continued development and commercialization.

"By providing each Harrington Scholar with a dedicated pharma team, we are able to de-risk the process for advancement to the clinic,” Dr. Jain stresses. “By the time the Scholar’s term is ending, the project has hopefully progressed to a stage where a strategic partner could step in to continue development.”

As proof, Harrington Discovery Institute’s five-year results include 74 projects supported to date at 41 institutions, five drugs accepted for investigational clinical use, 15 companies established - five of which have been licensed by major pharmaceutical companies.

The Harrington Project has received great interest from scientists around the globe, as well as from prominent disease foundations, academic institutions, philanthropic thought leaders, and global pharmaceutical companies. Yet, in Dr. Jain’s estimation, these first five years are only the prelude to future achievements from the Harrington Discovery Institute that will help shape a better world.

The 2017 Harrington Prize for Innovation in Medicine has been awarded to Daniel J. Drucker, MD, Mount Sinai Hospital, University of Toronto, Toronto, Canada; Joel F. Habener, MD, Massachusetts General Hospital, Boston, Massachusetts; and Jens J. Holst, MD, DMSc, University of Copenhagen, Denmark, for their 1984 discovery of incretin hormones and their subsequent development into breakthrough therapies for diabetes.

An Era of Discovery

At the time of the discovery, Dr. Drucker was a research fellow working closely with Dr. Habener in the latter’s lab at Massachusetts General. Together they discovered the actions of the incretin hormone GLP-1, which acts directly on the insulin-producing beta cells in the pancreas. They determined that GLP-1 stimulates insulin secretion from islet beta cells, helping glucose clearance after a meal.

Dr. Habener had been investigating how hormones and other small peptides are synthesized in cells for some time before finding GLP-1. “Through characterization of the gene encoding glucagon and glucagon-related peptides, we discovered that GLP-1 is synthesized in the intestine in response to eating and moves to the pancreas where it amps up insulin production,” he explains.

During the same period, Dr. Holst was conducting independent studies at his lab in Copenhagen, trying to identify insulinotropic hormones from the gut, when he found a new incretin hormone, GLP-1. Among other discoveries, Dr. Holst determined GLP-1’s activity in stimulating insulin secretion and inhibiting glucagon secretion, leading him to later identify its powerful action on blood glucose in humans.
From Bench to Clinic

Following the initial discovery, Dr. Drucker pursued basic and clinical studies supporting translation of GLP-1-related therapies for the treatment for Type 2 diabetes. The U.S. Food and Drug Administration 2005 approval of the first GLP-1-related drug, exenatide, was the culmination of two decades of science, dating back to the original work at Massachusetts General and the University of Copenhagen. In 2007 Dr. Drucker led the first Phase III trial for long-acting exenatide, the first once-weekly injection for Type 2 diabetes.

“I have spent several decades studying the activity of GLP-1 at the molecular level, hoping that it might one day help patients with diabetes or obesity,” Dr. Drucker says. In 2008 he published a scientific paper describing GLP-1's cardiovascular protective role in mice. In 2016, new studies in humans with diabetes have demonstrated that GLP-1 reduced heart attack, stroke and cardiovascular mortality in this population.

The Next Chapter

"The first 30 years of GLP-1 science have been fantastic," he says. “The beauty of GLP-1 is that it still has an exciting future, with new scientific discoveries on the horizon."

Dr. Habener likewise continues to study GLP-1, focusing now on the products of GLP-1 cleavage and their metabolic activity. "The story is still unfolding," Dr. Habener says. "That's why I am still working on GLP-1."

Drs. Drucker, Habener and Holst jointly delivered The Harrington Prize lecture at the 2017 Association of American Physicians/ASCI/American Physician Scientist Association Joint Meeting April 21. They also share the $20,000 honorarium and will publish an essay in The Journal of Clinical Investigation.

A committee comprising members of the ASCI Council and the Harrington Discovery Institute Scientific Advisory Board selected the 2017 recipients from 58 nominations from 49 institutions and five countries.

For more information please visit www.HarringtonDiscovery.org/ThePrize.
Harrington Fellows Program
Supports Cleveland-Area Physician-Scientists

The Harrington Fellows Program was created to recognize early-to-mid career physician-scientist faculty within the Cleveland academic community. In 2017, Harrington Discovery Institute is pleased to introduce the inaugural class of Harrington Fellows.

What is an Investigational New Drug Application?
Researchers conduct preclinical studies to determine if the potential new drug is reasonably safe for initial use in humans, and whether it has sufficient treatment potential to justify its commercial development. When these requirements have been demonstrated in animal studies, the next step is to test the product’s treatment potential in humans. At this stage, the drug developer submits an Investigational New Drug (IND) application to the U.S. Food and Drug Administration, requesting authorization to administer an investigational drug or biological product to humans. A researcher may submit an IND for a totally new, unapproved drug or for a new use of an existing, already approved drug.

Closing in on Crohn’s
Harrington Fellow Derek Abbott, MD, PhD, gets a close-up view of dozens of different diseases every day as a pathologist at Case Western Reserve University School of Medicine. He finds the human GI (gastrointestinal) tract and the diseases that affect it a source of ongoing wonderment. “When you think that all that keeps us from being sick all the time with GI diseases is a single layer of cells, it’s amazing,” he says.

This fascination, coupled with compassion for patients who suffer every day with chronic GI diseases, inspired him to pursue research into Crohn’s disease, an incurable inflammatory disease of the GI tract.

A hyper-immune response in the intestinal tract creates the inflammation and tissue destruction that characterize the disease. Four years ago, Dr. Abbott partnered with a biotechnology company to synthesize a compound to inhibit this response and has been working to improve it.

“We think the end is in sight,” he says. “But we are in the Valley of Death and trying to climb out.” Dr. Abbott looks to the Harrington Discovery Institute to give him and his team the lift they need to climb out of the valley and into the clinic.

From Challenges Come Cures
Even a brief conversation with pediatric cancer specialist Alex Huang, MD, PhD, is enough to detect his dedication to his research, especially its potential for treating children with brain tumors and sarcoma. “My passion comes from research and finding translational opportunities to tackle difficult problems.”
Dr. Huang is collaborating with 2017 Harrington Scholar-Innovator John J. Letterio, MD, Director of the Angie Fowler Adolescent & Young Adult Cancer Institute, in the development of a treatment for pediatric brain tumors. Their treatment would inhibit a biologic pathway that lets tumors avoid the body’s immune system, resist chemotherapy and spread.

Drs. Huang and Letterio believe their work also may have potential as an immunotherapy for sarcoma in children that has spread throughout the body. “These are serious issues in kids that drive me,” Dr. Huang adds. “If we could develop a cure or prevent relapse with minimal side effects that would be remarkable.”

**Compassion for Patients Inspires Research**

Nima Sharifi, MD, is a man with a mission. He studies the underlying molecular machinery that allows prostate tumors to become resistant to treatment. One of his team’s major discoveries was a specific genetic mutation that causes men who have it to develop resistance to prostate cancer treatment.

Dr. Sharifi plans to use that mutation as a biomarker to identify prostate cancer patients likely to develop resistance to hormone therapy, a treatment often used in advanced prostate cancer or prostate cancer that has spread to other sites in the body. With Harrington Discovery Institute support, Dr. Sharifi will develop a clinical trial specifically for this group of patients.

As a medical oncologist, Dr. Sharifi has cared for hundreds of men with advanced metastatic prostate cancer. “Seeing these patients and developing a rapport with them – knowing there is no treatment for metastatic disease – drew me to this field of research,” he says.

“Success will be when our discoveries change how we manage patients for the better with a biomarker or a new drug.”
HARRINGTON SCHOLAR-INNOVATOR AWARD:

Supporting BREAKTHROUGH DISCOVERIES

The Harrington Scholar-Innovator Award recognizes physician-scientist innovators throughout the U.S. whose research has the potential to change standard of care. The Scholar-Innovator Award provides funding and drug development support to help bridge the gap between basic discovery and the clinic.

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.
**Old Drug, NEW TARGET**

**PAUL L. BOLLYKY, MD, PHD**
Assistant Professor, Department of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Stanford, California

**FOCUS**
Repurpose an existing drug for the prevention of Type 1 diabetes (T1D), an autoimmune disease that destroys the pancreatic islets, the tiny clusters of cells in the pancreas that produce insulin

**Goals**
Dr. Bollyky is engaged in repurposing the drug hymecromone, approved for more than 50 years in Europe and Asia for gallstone prevention, to prevent and possibly treat Type 1 diabetes. The Bollyky lab has demonstrated that hyaluronan, a component of inflamed tissues, builds up in the pancreatic islets in individuals at risk of Type 1. The Bollyky lab subsequently showed that the accumulation of hyaluronan is able to override the body’s normal protection against autoimmune attack and is essential for development of Type 1 diabetes. They found that hymecromone inhibits hyaluronan production, thereby preventing the autoimmune attack on the pancreas. Along with demonstrating the effectiveness of hymecromone in diabetes prevention, Dr. Bollyky is looking to Harrington Discovery Institute for assistance in formulating hymecromone as a once-a-day pill for maximum effectiveness.

**From the Scholar-Innovator**
“If we can figure out how inflamed tissues communicate with the immune system, we can modulate the signals that drive autoimmunity and teach the body not to attack itself.”

“Our vision is to develop an oral pill for children at risk of T1D that will prevent the disease.”

“I have a personal interest in autoimmunity – a number of people in my family have T1D or other autoimmune diseases. I feel incredibly lucky to be able to pursue research questions that are personally meaningful, scientifically compelling and may potentially have a broad impact on patient health.”

**Milestones**
2014 Discovered that hyaluronan deposits are present in the pancreas of patients with Type 1 diabetes and override normal protection from autoimmune damage

2015 Tested hymecromone in preclinical models, proving that it inhibits the accumulation of hyaluronan and prevents development of autoimmunity

2016 Selected as a Harrington Scholar-Innovator
FOCUS

Develop a small-molecule therapeutic that prevents drug resistance in Staphylococcus aureus, a common cause of community and hospital-acquired infections

Goal

Dr. Cheung plans to progress the small molecule DNAC-23a or its analogs through preclinical studies to identify its target in methicillin-resistant S. aureus (MRSA), study its pharmacodynamics and develop the optimal compound for further testing. The Cheung lab screened 60,000 small molecules and identified DNAC-2 as a compound that inhibited the growth of MRSA. One of its analogs, DNAC-23a, appears to have synergistic killing activity with oxacillin, a form of penicillin commonly given to treat Staph infections, but its target and toxicity were unknown. With Harrington Discovery Institute support, Dr. Cheung believes he can move DNAC-23a and its analogs to a Phase 1 trial.

From the Scholar-Innovator

“As an infectious disease physician, I have been aware of the problem of drug resistance. We know that many drugs that were effective are no longer useful in treating infections such as Staph aureus.”

“The question was whether we could find a compound that would work with existing drugs that used to be effective to make them effective again. In this case, we have found a compound that we can combine with oxacillin and be effective in MRSA.”

“Being an MD researcher, I bring a different perspective to research. I try to do research that is useful. I am always looking for things that make a difference to patients.”

Milestones

Discovered DNAC-2, a compound that inhibits MRSA

Synthesized DNAC-23a, a small molecule that does not act against MRSA on its own but is deadly in combination with oxacillin, a proven drug against Staph

Evaluated DNAC-23a and its analogs for their pharmacokinetics and identified its desirable characteristics such as solubility and lack of toxicity

More about MRSA

In recent years, infection with methicillin-resistant Staphylococcus aureus – better known as MRSA – has become a national and international health concern. MRSA is a bacteria that causes an infection, which is now resistant to treatment with an antibiotic that was used for many years to treat Staph infections. Most MRSA infections develop in hospitalized patients.

According to the Centers for Disease Control and Prevention, Staphylococcus aureus (including MRSA) caused about 11 percent of healthcare-associated infections in 2011. More than 290,000 hospitalized patients develop a Staphylococcus aureus infection each year, and approximately 126,000 of those are MRSA.

Most cases of MRSA can be cleared up by other antibiotics. For some patients, particularly the elderly, dialysis patients and those who are frail due to other diseases, MRSA can cause serious complications. These include tissue death, other infections throughout the body and kidney failure.
HarringtonDiscovery.org

**TARGETING A KILLER:**

Pancreatic Cancer

**Goals**

Dr. Draetta’s team has identified the enzyme arginine methyltransferase PRMT1 as a critical regulator of growth in pancreatic cancer, a disease recalcitrant to treatment due to the presence of KRAS and p53/SMAD4 mutations. They have generated potent and specific inhibitors of this enzyme and are assessing their mechanism of action and efficacy in disease models. With the support of the Harrington Discovery Institute’s Innovation Support Center, the team aims to identify a suitable drug candidate to move forward into clinical development and to dissect the underlying biological mechanisms that drive response to PRMT1 inhibition. Dr. Draetta and his team are planning to submit an Investigational New Drug Application to the United States Food and Drug Administration within two years.

**From the Scholar-Innovator**

“I have devoted my career to cancer genetics and translational medicine. Even with the incredible scientific advancements of recent years, our ability to provide patients with cancer therapies that can dramatically impact the course of their disease remains inadequate. The gap in time between scientific discovery and viable therapeutic modality is unacceptably long, and often spans decades. With the Harrington Discovery Institute’s help, we hope to shorten that cycle dramatically.”

“We use a state-of-the-art in vivo platform to interrogate the functional cancer genome toward identifying druggable vulnerabilities within very specific disease contexts. With this approach, we not only uncover novel cancer dependencies, but we are poised to deeply understand the biological reasons why a tumor depends on a particular gene product. This project was born from this platform upon our discovery that PRMT1 inhibition dramatically blocked the growth of human-derived pancreatic adenocarcinoma models, and we are making important progress towards understanding why that is the case.”

“Our model of academic drug discovery requires active fundraising. We wish to keep our programs at least initially independent of the biotech and pharmaceutical industry – relying on the world-class scientific resources of the M.D. Anderson Cancer Center and their top-notch faculty and clinicians – to maintain our focus on clinical need and biological relevance. This is our mission, to ensure that the drugs we deliver to our patients have the highest possible impact on disease.”

**Milestones**

Proved that compounds are available that mimic the deactivation of a specific gene (PRMT1) essential to the growth of pancreatic cancer

Demonstrated that these compounds inhibited PRMT1 in animal models and elucidated their mechanisms of action.
FOCUS
Develop a new class of cancer drugs that target a newly discovered molecular pathway

Goals
The Field lab has discovered a molecular pathway that involves a protein, GOLPH3, which promotes tumor growth and survival. Dr. Field’s team have demonstrated that inhibiting GOLPH3 with various small molecules prevents tumor growth and kills cancer cells. With guidance from the Harrington Discovery Institute’s Innovation Support Center, Dr. Field and his team aim to determine how their small molecules inhibit GOLPH3, prove their efficacy against cancer cells and screen additional small molecules to identify those with the greatest potential to be advanced.

From the Scholar-Innovator
"Our data from the lab demonstrate that interfering with GOLPH3 preferentially kills cancer cells. But getting from there to human beings is a long way."

"A homerun would be developing a drug that saves people’s lives. If we could impact even a subset of patients, that would be great."

"New drugs and what we learn along the way are powerful tools that help us understand cancer and can lead to new ways of thinking about cancer and its treatment."

Milestones
2009 Discovered a biologic pathway that is key to the function of the Golgi apparatus, a structure in the cell that packages proteins and fats for transport out of the cell. GOLPH3 plays a critical role in the function of the Golgi apparatus.

2009 Determined that this pathway is related to cancer

2010 Began considering development of GOLPH3 inhibitors as a cancer therapeutic

2014-2017 Discovered GOLPH3’s mechanism of action in cancer, involving DNA damage and cell migration
FOCUS
Develop a new, fast-acting treatment for clinical depression that relieves symptoms without side effects

Goals
Ketamine, a long-established anesthetic, is known to have fast-acting antidepressant effects. Its use as a depression treatment is limited, however, because of side effects including dissociation and abuse potential. The Gould lab discovered ketamine’s antidepressant effects are actually due to one of its metabolites, 2R,6R-HNK. In mice, this molecule is a rapid-acting antidepressant without the side effects of ketamine. With support from Harrington Discovery Institute, the Gould lab aims to conduct further studies of 2R,6R-HNK to be better positioned for U.S. Food and Drug Administration approval.

From the Scholar-Innovator
“I have always been passionate about medical research and wanted to develop new drugs.”

“This is a team effort that involves academics, Harrington Discovery Institute’s industry experts and individuals at NIH (National Institutes of Health) as equal partners in discovery and development.”

“We are convinced that our drug has potential, but we are cognizant of recent history in the neurosciences where new drugs work in animal models but not in humans.”

Milestones
2016 Published results in Nature, offering scientific evidence that 2R,6R-HNK has antidepressant activity without side effects
FOCUS
Advance a first-in-class small-molecule therapeutic that inhibits an enzymatic regulator of pathways essential for the growth and spread of cancer.

Goals
The enzyme cyclin dependent kinase 5 (Cdk5) is very active in cancer cells, enabling them to evade detection by the immune system, resist the effects of chemotherapy drugs and spread throughout the body. The Letterio lab has developed MDX01, a highly specific inhibitor that disrupts distinct molecular interactions required for Cdk5 activation and function. With support from Harrington Discovery Institute, the Letterio lab will advance studies of MDX01 through the preclinical stage and complete the formulation and characterization work necessary to pursue an Investigational New Drug application.

From the Scholar-Innovator
"Advances in science and medicine have enabled a giant leap forward in our understanding of the biology of rare diseases, like childhood cancer. We have an obligation to use that information to make a difference. That is what motivates me."

"Cdk5 has emerged as an important therapeutic target in some of the most serious cancers affecting both adults and children, including brain tumors and cancers with a high propensity to spread or metastasize. However, we think the potential, broader impact of this effort is quite high as our own data also reveal a critical role for Cdk5 in forming immune memory, a function that predicts application of MDX01 in settings that include autoimmune disease and organ transplant. We have had many physician-scientists calling, interested in how MDX01 could help patients affected by many diseases where Cdk5 is viewed as a therapeutic target."

"We are very focused on the impact of this effort, as our advances in the laboratory only truly matter if they lead to better outcomes for the patients and families affected by these conditions."

Milestones
2010 Disrupted Cdk5 gene expression in immune cells, demonstrating that CDK5 inhibition is protective in preclinical models of neurodegeneration and multiple sclerosis
2015 Revealed Cdk5 as an inhibitor of ‘suppressor’ or regulatory immune cell development
2016 Developed MDX01, a Cdk5-specific inhibitor, shown to suppress growth of cancer cells
2017 Reported first evidence that disruption of Cdk5 activity prevents development of deadly graft-versus-host disease (transplant rejection) in preclinical models of bone marrow transplant

JOHN J. LETTERIO, MD
Jane and Lee Seidman Chair of Pediatric Cancer Innovation; Chief, Pediatric Hematology Oncology; Director, Angie Fowler Adolescent & Young Adult Cancer Institute, University Hospitals Cleveland Medical Center and UH Rainbow Babies & Children’s Hospital; Professor, Pediatrics, Case Western Reserve University School of Medicine, Cleveland, Ohio
Pathway to Progress in FIGHTING MELANOMA

DAVID B. LOMBARD, MD, PHD
Associate Professor, Department of Pathology; Research Associate Professor, Institute of Gerontology, University of Michigan, Ann Arbor, Michigan

FOCUS
Develop new treatments for metastatic melanoma

Goals
The Lombard lab proposes development of new therapies that inhibit the mechanism that prevents cell death in melanoma. The team is focusing on an anti-cell-death gene that is present in more than half of melanoma patients as a therapeutic target. Now, they hope to advance one of three new compounds that have been shown to have activity against that gene in the laboratory. Through the assistance of Harrington Discovery Institute and its Innovation Support Center, Dr. Lombard and his co-Principal Investigator Zaneta Nikolovska-Coleska, PhD, Associate Professor of Pathology, aim to conduct preclinical trials of their lead compound to test its effectiveness and safety when given alone and in combination with other anti-melanoma drugs.

From the Scholar-Innovator and his co-PI
“There has been tremendous progress in treating metastatic melanoma, but many patients still succumb to this disease because they are resistant to treatment. We are taking a different approach by targeting the cell death pathway.”
– Dr. Lombard

“We have developed a class of potent and selective inhibitors of a protein called Mcl-1 (myeloid cell leukemia 1) that regulates the cell death pathway. This anti-cell-death protein has been validated as a major factor in explaining why patients become resistant to treatment. Novel small-molecule inhibitors block the interactions between Mcl-1 and pro-death proteins and specifically kill melanoma cell lines.”
– Dr. Nikolovska-Coleska

Future Milestones
2017 Optimize the most promising Mcl-1 inhibitors to further improve binding affinity, physicochemical properties, and oral bioavailability

2017 Characterize novel designed and synthesized analogs at the biochemical, biophysical, functional and cellular levels using panels of melanoma and normal cells

2018 In vitro (in the lab) and in vivo (in live subjects) efficacy evaluation of the most potent Mcl-1 inhibitors as single agents and their combination with standard melanoma treatments

“We believe that the Harrington Discovery Institute will turbocharge our efforts.”

David B. Lombard, MD, PhD
FOCUS

Improve radiation therapy and chemotherapy effectiveness through development of a new class of compounds that target a specific DNA repair pathway and sensitize tumors to treatment in a multitude of human malignancies.

Goals

Radiation therapy and chemotherapy act by damaging DNA. A biologic pathway, the NHEJ pathway, is very active in many types of tumors and promotes DNA repair at double-strand breaks, but with errors. The resulting unstable DNA – a characteristic of cancer – can make the tumor resistant to treatment. Dr. Mahadevan and his team have identified Ku70/80, a protein that plays a pivotal role in the NHEJ process, as a potential therapeutic target in the pathway. What’s more, using state-of-the-art, computer-based screens, they also have discovered a novel small molecule that interferes with this target and pathway. As a Harrington Scholar-Innovator, Dr. Mahadevan hopes to connect with experts who can contribute to the rational design of small-molecule Ku70/80 inhibitors, evaluate the molecule’s activity in preclinical models and investigate its efficacy, safety, pharmacokinetic and pharmacodynamics properties in mouse models of cancer, including glioblastoma (brain cancer) and prostate cancer.

From the Scholar-Innovator

“We are working with structural biologists, medicinal chemists and radiobiologists to evaluate small-molecule inhibitors based on the original molecule (compound L). Currently we have generated 15 novel chemical entities and are testing these in a validated series of assays. Real progress has been made with compound improvement in activity, binding and solubility.”

“Crystallography is the next step, which will prove how the drug binds to the Ku70/80 DNA-repair protein and may impact DNA binding to the protein. Once we have that information, we could be on to a winner.”

“In my practice as a clinical trials physician, I see cancer patients who have failed standard-of-care therapies and are seeking novel, first-in-class, investigational agents or combinations to prolong life and to help advance clinical research. Most of them are going to progress or die while on these trials, but my patients inspire me to find new treatments that will prolong life, as well as, provide for a good quality of life.”

Milestones

2012 Began searching for a drug that targets Ku70/80 at request of a radiation biologist Eric Weterings, PhD, Assistant Professor, Medicine – (Research Scholar Track) and Assistant Professor, Radiation Oncology, University of Arizona College of Medicine

2014 Applied state-of-the-art, computer-based screens to identify nine potential lead-like small-molecule inhibitors targeting Ku70/80-DNA double strand interactions

2015 Demonstrated that two of the small-molecule inhibitors specifically interfered with Ku70/80 binding to DNA

2016 Sensitized compound L, a small-molecule inhibitor, with radiation in glioma, prostate and pancreas cancers

2016 Published manuscript reporting on this novel small-molecule Ku70/80 inhibitor
FOCUS
Discover new small molecule strategies to target cancer-causing proteins

Goals
CD437 was identified as a cancer-specific toxin nearly 20 years ago. CD437 causes complete cell death of cancer but not normal cells. In spite of its promise, CD437 has not been advanced into clinical trials because its protein target remained unknown. The Nijhawan lab discovered that CD437 acts by binding to the enzyme DNA polymerase alpha (POLA1). POLA1 is required for DNA replication, and inhibition of POLA1 in cancers leads to cell death. With knowledge of the CD437 target, the Nijhawan lab, with support from Harrington Discovery Institute, is poised to optimize its structure and action. Dr. Nijhawan is seeking expertise and guidance from the Harrington Discovery Institute’s Innovation Support Center experts on the design of a POLA1 inhibitor as a first-in-class drug.

From the Scholar-Innovator
“Every patient I see dies. Most of my patients have few treatment options, and in many cases, they are getting the same medications that their parents would have received. We are trying to find new ways to target cancer-causing proteins to develop new treatments and discover something different.”

“Finding the protein target of a cancer toxin is an incredibly interesting problem. A compound causes cells to die by targeting one of nearly 20,000 proteins. Which one is it? We enjoy the hunt.”

“I am very much a physician-scientist, but I am a pure scientist as well. There are hundreds of small molecules that kill cancer. We take these molecules and try to discover their protein targets in the cell.”

Milestones
2013 Discovered four new proteins that are potential targets for new cancer drugs
2013 Awarded a three-year grant by the Damon Runyon Cancer Research Foundation to investigate CD437 as a cancer treatment
2015 Identified POLA1 as the antitumor target for CD437
2016 Received a two-year continuation grant to further his research on CD437, considered a promising new cancer therapeutic
A Natural Approach to TREATING SICKLE CELL

STUART H. ORKIN, MD
David G. Nathan Professor of Pediatrics, Harvard Medical School, Dana-Farber Cancer Institute and Boston Children’s Hospital; HHMI Investigator, Boston, Massachusetts

FOCUS
Discovery of natural products that activate production of fetal hemoglobin as treatment for sickle cell disease

Goals
Fetal hemoglobin, the form of hemoglobin naturally present in an infant from the second month of gestation through the first six months of life, inhibits the collection of abnormal hemoglobin found in sickle cell disease. Certain natural compounds, such as those derived from marine microbes, have been observed to disrupt the biologic pathway that suppresses fetal hemoglobin production. With support from Harrington Discovery Institute, the Orkin laboratory aims to purify and characterize the biologic activity of two natural extracts that reactivate fetal hemoglobin by interfering with the function of a protein that normally contributes to fetal hemoglobin silencing.

From the Scholar-Innovator
“Years of intensive basic science have laid the foundation for the work we are doing now. This is the culmination of three decades of molecular biology work.”

“Our aim has been to find molecules that disrupt the pathway that results in silencing of the fetal hemoglobin gene, thereby reactivating fetal hemoglobin. A fetal hemoglobin level that is 15-20% of total hemoglobin is sufficient to prevent sickle cell disease.”

Milestones
1980s-1990s Gained understanding of the molecular biology of hemoglobin disorders
2008 Discovered BCL11A and LRF (2016), the two most potent suppressors of fetal hemoglobin
2016 Proved the activity of these two suppressors and validated them as regulators of fetal hemoglobin production

“Sickle cell disease is a blood disease characterized by production of a mutant version of adult beta-hemoglobin, the “red” protein in blood that carries oxygen.”
New Treatment to HELP KIDS Overcome a Killer

FOCUS
Develop a treatment for Niemann-Pick type C (NPC), a rare, fatal, pediatric neurodegenerative disease characterized by excessive cholesterol storage throughout the nervous system.

Goals
In NPC, misfolded proteins trigger a series of events at the molecular level that result in loss of nerve cells in the brain. The Ory lab aims to develop a small molecule that targets a protein-folding pathway, causing proteins to fold correctly and move to their correct location in the cell. With support from Harrington Discovery Institute, Dr. Ory hopes to develop the next generation of drugs for NPC, potentially targeting the protein-folding pathway.

From the Scholar-Innovator
“We realized that we really needed to couple development of a treatment with early diagnosis. If you can treat early, you can prevent or delay the onset of the disease. The result was a new biomarker for newborns, currently being piloted by the New York State Department of Health.”

“We work very closely with patient advocacy groups, which are comprised of very special families who want to partner with scientists to make a difference.”

“I am a cardiologist by training and began working on NPC as an accident. We found a defect in cholesterol self-regulation in certain cells, and those cells were cells from NPC patients. We became curious about NPC, and our work became focused on it.”

Milestones
2006 Work of National Institute of Child Health and Development Senior Investigator Forbes “Denny” Porter, MD, PhD, established disease progression in patients and created a biorepository to identify biomarkers for disease progression

2010 Identified an oxidized cholesterol (C-triol) as a biomarker for Niemann-Pick type C

2011 Developed an assay for diagnosing Niemann-Pick type C that delivers results overnight from a single drop of blood

2011 NPC selected as pilot program by National Institutes of Health (NIH) Therapies for Rare and Neglected Disease with Dr. Ory as Principal Investigator to develop cyclodextrin as a therapy

2013 Phase 1/2a trial of intrathecal (injected into the spine) cyclodextrin (VTS-270) begun at NIH

2015 Phase 2b/3 trial of intrathecal VTS-270 began enrollment

2016 Discovered novel bile acid biomarker for NPC and developed newborn screening test
Partnerships Expand Harrington Discovery Institute’s Impact

From the beginning, Harrington Discovery Institute knew it would need mission-aligned partners to accelerate the advancement of novel discoveries and impact the pace of drug development. In its five year history since founding, Harrington Discovery Institute has developed four strategic partnerships. In 2014, Harrington Discovery Institute launched collaborations with Alzheimer’s Drug Discovery Foundation (ADDF) and the University of Oxford. In 2015, another award program and the first Center for Excellence followed shortly thereafter in conjunction with the Foundation Fighting Blindness (FFB). These initiatives expanded support to PhD researchers in addition to MD’s in targeted therapeutic areas, introduced Harrington Discovery Institute’s model to the United Kingdom, and provided more resources from the collaborative efforts. In addition to funding, all partner scholars receive hands-on drug development guidance and project management from pharmaceutical industry leaders through the Innovation Support Center, the signature element of Harrington Discovery Institute. To date, 19 partner scholars have been selected with more to be awarded later this year.

Most recently in April 2017, Harrington Discovery Institute announced a multi-year partnership with Japan-based Takeda Pharmaceutical Company to accelerate breakthrough therapeutic discoveries in rare diseases. Up to ten Harrington Rare Disease Scholars will begin their terms in 2018, creating the largest Harrington Discovery Institute partner scholar class to date. This collaboration will help to bridge academia and industry and leverage the partners’ financial and human capital to achieve their joint mission.

“The route from discovery through development to ultimately the patient is not a marathon, but a relay race. Our engagement on these discovery projects is for a fixed term of two years and so, we are always looking for partners to hand off to, so they can continue to gather momentum and advance these programs,” said Shobha Parthasarathi, Vice President, Strategic Alliances and Business Development. As Harrington Discovery Institute celebrates its five-year anniversary, the organization continues to move ahead with new programs, partners, and funding structures for long-term impact. “Our model has sparked interest from across the spectrum of possible collaborators – academia, private foundations, accelerators, clinical research organizations and large pharmaceutical companies” remarked Dr. Parthasarathi. “We are developing new business models with organizations that share our sense of urgency and vision to transition large numbers of drug discovery projects into clinical development. It is an exciting time at Harrington Discovery Institute.”
Partner Scholar Programs Advance DISCOVERIES

ADDF-HARRINGTON SCHOLAR AWARD
Advancing Discoveries in Alzheimer’s disease
In partnership with the Alzheimer’s Drug Discovery Foundation (ADDF), the ADDF-Harrington Scholar Award recognizes scientists across the U.S. who are doing research to develop drugs to prevent, treat, and cure Alzheimer’s disease. The award provides funding and drug development support to help bridge the gap between basic discovery and the clinical realm.

Meet the 2016 ADDF-Harrington Scholars on pages 28 and 29

GUND-HARRINGTON SCHOLAR AWARD
Advancing the Development of Vision Restoring Therapies
Foundation Fighting Blindness and Harrington Discovery Institute have partnered to form the Gund-Harrington Scholar Award program. The award provides funding and drug development support to innovative research efforts that could prevent, treat or cure blindness.

Meet the 2016 Gund-Harrington Scholar on page 30

OXFORD-HARRINGTON SCHOLAR AWARD
Supporting Breakthrough Discoveries in the U.K.
In 2014, the Oxford-Harrington Scholar Award was launched to support physician-scientists at the University of Oxford and elsewhere in the U.K. who are working on novel drug discovery research. The University of Oxford and the Harrington Discovery Institute combine their expertise and resources to help advance these drug discovery projects into new medicines.

Meet the 2016 Oxford-Harrington Scholar on page 31

HARRINGTON RARE DISEASE SCHOLAR AWARD
Accelerating the Development of Cures and Therapies for Rare Diseases
Established in 2017, this program is sponsored by Takeda Pharmaceutical Company Limited and overseen by Harrington Discovery Institute. The Harrington Rare Disease Scholar Award will provide funding and hands-on drug development guidance for two years to U.S. based PhD and MD researchers whose discoveries show promise for translation into novel medicines for rare disease. The inaugural class of up to 10 Harrington Rare Disease Scholars will be selected in early 2018.

Learn more about the Takeda - Harrington collaboration on page 38
Untangling the CAUSE of Alzheimer’s Disease

TRAVIS DUNCKLEY, PHD
Assistant Research Professor, ASU-Banner Neurodegenerative Disease Research Center, Arizona State University, Tempe, Arizona

FOCUS
Advance development of a new small molecule that inhibits activity of the enzyme DYRK1A as a novel treatment for Alzheimer’s disease

Goals
Dr. Dunckley is investigating tau protein in the brain as a viable therapeutic target in Alzheimer’s disease. Tau protein is known to undergo numerous abnormal chemical modifications, caused in part by the enzyme DYRK1A. The aberrant proteins stick together to create neurofibrillary tangles, a hallmark of Alzheimer’s disease. The tangles disrupt neurons’ normal activities, block signals between neurons and eventually cause neuronal death. Formation of amyloid plaques in the brain, another characteristic of Alzheimer’s disease, precedes tangle formation and is believed to exacerbate their development and also contribute to neuronal death. Dr. Dunckley and his team have identified a DYRK1A inhibitor that reduced tau proteins by 40 percent and amyloid plaques by 50 percent in preclinical models. Dr. Dunckley is seeking expert guidance from Harrington Discovery Institute’s Innovation Support Center experts on the metrics needed to interest a pharmaceutical company or other investor and progress this small-molecule DYRK1A inhibitor to the clinic.

From the ADDF-Harrington Scholar
“Alzheimer’s is such a horrific disease, and there is a huge need for effective treatments because none are currently available. DYRK1A is a relatively new and promising target that directly addresses the underlying pathologies of this disease.”

“Once the cascade begins in the brain with the modification of the tau proteins and neuronal death, it is difficult to reverse the changes. That is why we are targeting the underlying process – the aberrant phosphorylation of the tau proteins – that initiates the cascade.”

“At this stage, meeting with knowledgeable advisors from Harrington will be the next measure of our success. The experts associated with Harrington are extremely valuable because of their market awareness and knowledge of the commercial aspects required for successfully advancing a new molecule to the clinic. As an academic scientist, that part of drug development is totally unknown to me.”

Milestones
Measured changes in tau proteins and identified the enzyme DYRK1A that causes their modification and formation of neurofibrillary tangles in the brain

Proved that reversing DYRK1A’s action improved memory in animal models

Partnered with the Arizona Alzheimer’s Research Consortium in a preliminary trial of a small-molecule DYRK1A inhibitor that reduced tau proteins by 40 percent and amyloid plaques by 50 percent in an animal model

To read more about Dr. Dunckley’s project please turn to page 33.
ABNORMAL PROTEINS
and Alzheimer’s Disease

FOCUS
Determine the best drug candidate as a potential treatment for Alzheimer’s disease from among several possible molecules the Yoon lab has identified.

Goals
The enzyme JNK3 is known to add an extra phosphate to a cellular protein in the brain to create an abnormal protein. In the brains of people with Alzheimer’s disease, JNK3 is very active, and the resulting aberrant protein appears to disrupt the normal processes that keep cells in metabolic balance. When JNK3 is deleted genetically in laboratory animals, the amount of abnormal protein is reduced by 90 percent. Dr. Yoon seeks a small-molecule inhibitor of JNK3. Dr. Yoon and her colleagues have identified several potential candidate molecules. With assistance from Peter Bernstein, PhD, a member of the Harrington Discovery Institute’s Innovation Support Center Advisory Board, they hope to determine the best candidate for further development.

From the ADDF-Harrington Scholar
"Metabolic disruption has been observed as a common theme in many chronic diseases. Interestingly, patients with Type 1 diabetes, a metabolic disease, develop Alzheimer’s at twice the rate of non-diabetics. If we can discover how metabolism is disturbed in Alzheimer’s, there potentially could be other applications for this drug.”

“We are curious, asking what is behind this metabolic disruption. We now may have a hint, which leads to a totally different kind of research. It comes with a challenge, but that is what keeps us going.”

Milestones
Demonstrated that genetically deleting the enzyme JNK3 in animal models protects against development of abnormal proteins associated in humans with Alzheimer’s disease.

Future Milestones
Identify a lead candidate that will be stable in biological systems.
Advance the understanding of that compound and its activity.
Develop medicinal chemistry of the lead compound.

SUNG OK YOON, PHD
Associate Professor, Biological Chemistry and Pharmacology; The Ohio State University College of Medicine, Columbus, Ohio

Alzheimer’s disease is the sixth leading cause of death in the United States and accounts for 60 to 80 percent of all dementias. Available treatments temporarily slow the pace of cognitive decline and improve the quality of life for Alzheimer’s patients. There currently is no cure for Alzheimer’s.
Goals
The disease process in retinitis pigmentosa and other blinding disorders involves the degeneration of the retina’s rods and cones, the photoreceptor cells that are essential to vision. This process causes progressive vision loss in the affected individual. Dr. Gamm and his colleagues have developed a method and technology to grow functional, three-dimensional tissues containing rods and cones from human stem cells in a dish. The next challenge for progressing this technology will be delivering and inserting the rods and cones into the eye in the proper alignment using a photoreceptor-seeded scaffold. Dr. Gamm anticipates that the Gund-Harrington award will advance the project by supporting his collaboration with University of Wisconsin engineers to solve the delivery challenge.

What is a photoreceptor-seeded scaffold?
Tissue engineering often combines cells with physical supports and biochemical signals that together comprise a cell scaffold. Such scaffolds are designed to support cell delivery, survival and integration. For Dr. Gamm’s purposes, the ideal scaffold is made of biodegradable material that can be populated with precursor cells that will mature into rods and cones when placed in the eye.

FOCUS
Apply human stem cell technology to the study and treatment of inherited and acquired degenerative retinal diseases, a significant cause of incurable blindness worldwide.

“"We and others are able to take a skin or blood sample and, through a series of steps, generate an unlimited supply of retinal cells from any individual. This never ceases to amaze me."

“As a pediatric eye surgeon I diagnose and treat many kinds of inherited retinal disease. The most frustrating are the ones I cannot do anything about. To be part of taking this work forward in an effort to help patients and families is what gets me up in the morning.”

Milestones
2008 Devised the technology to grow three-dimensional photoreceptor structures in the laboratory
2011 Published paper in *Stem Cells* reporting first use of human-induced pluripotent stem cells to grow early retina-like structures in the laboratory using skin cells of a patient with a blinding disease
2013 Teamed with engineers to develop the photoreceptor-seeded scaffold to carry rods and cones for insertion into a human eye

From the Gund-Harrington Scholar
“When (University of Wisconsin scientist) James Thomson pioneered human embryonic stem cells in 1997, I saw the promise and possibility of taking his discovery in a direction that could be relevant and make a difference for the patients for whom there are no treatments.”

Stem Cells to CONQUER BLINDNESS

DAVID M. Gamm, MD, PHD
Associate Professor Ophthalmology and Visual Sciences; RRF Emmett A. Humble Distinguished Director, McPherson Eye Research Institute; Waisman Center Stem Cell Research Program; University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin
FOCUS
Develop a small-molecule therapeutic that blocks insulin-like growth factors (IGFs) to treat and prevent cancer

Goal
Insulin-like growth factors (IGFs) are hormones produced by the liver that regulate growth and development. IGFs are closely related to insulin, which enables the body to utilize glucose. By binding to receptors on the surface of cancer cells, IGFs promote cancer growth and resistance to treatment. It has been found that people born with a genetic mutation (Laron syndrome) that prevents IGF production do not develop cancer. In the general population, people with high IGF are at increased risk of cancer. Dr. Macaulay and her team are investigating the role of IGFs in cancer and also are testing anti-IGF drugs made by various pharmaceutical companies. They are now seeking small-molecule drugs that block IGFs in new ways, aiming to re-sensitize tumors to anti-cancer drugs or radiation therapy, and ultimately to prevent cancer development. As an Oxford-Harrington Scholar, Dr. Macaulay hopes to identify a potential drug candidate and advance it through preclinical and clinical trials.

From the Oxford-Harrington Scholar
“This work keeps raising new questions. You have to be very motivated and be prepared to work hard to overcome obstacles and delays.”

“It is a privilege to look after patients, and to be involved in trials of anti-IGF drugs. Sometimes patients come over to visit the lab – this helps the patients to understand how we are working to improve treatment. Meeting patients is also very inspiring for the scientists in my lab.”

“The ultimate aim of cancer research is prevention. It is possible that blocking IGFs could reduce the risk of cancer, and I am keen to pursue this.”

Milestones
Dr. Macaulay’s team showed that IGFs help to make cancers resistant to anti-cancer treatments, including radiotherapy.

2010-current The team found that IGF receptors can move into the nucleus of cancer cells, switching on genes that make cancers behave aggressively.

2017 and on Dr. Macaulay’s team is investigating new ways to block IGF actions in cancer cells without affecting insulin actions on glucose.

To read more about Dr. Macaulay’s project please turn to page 34.
“Secret Sauce” Delivers the INGREDIENTS FOR SUCCESS

Driven by Success

“All Innovation Support Center members have had experience with projects coming to fruition,” explains Diana R. Wetmore, PhD, Vice President, Therapeutics Development and Director, Innovation Support Center. “Getting drugs approved motivates them, and their desire for another’s success drives them.”

Every Harrington Scholar is paired with an Innovation Support Center coordinator, based on the needs of the Scholar’s drug discovery project. In a very collaborative relationship, the coordinator enlists other Innovation Support Center Advisory Panel members to meet the Scholar’s specific needs as the project unfolds.

The Innovation Support Center’s goal, Dr. Wetmore stresses, is to transition as many projects as possible to the next step. For many that means further development by BioMotiv, the for-profit, mission-aligned accelerator associated with The Harrington Project. Once the BioMotiv Board of Managers votes to add a project to its portfolio, BioMotiv partners closely with Harrington Scholars and their academic institutions to form companies around their breakthrough discoveries.

That combination of scientific knowledge with pharma industry savvy appears to be a winner. In its first five years, Harrington Discovery Institute already has seen 11 projects successfully licensed to commercial partners, including five to BioMotiv, and progressed four discoveries to clinical readiness. And with a bit more of that secret sauce, several others soon will be there.
Progressing Towards a New Drug

The Harrington Discovery Institute’s Innovation Support Center is tasked with providing drug development and commercialization guidance to help Harrington Scholars bridge the academic-industry divide. Innovation Support Center Advisory Panel member Patricia C. Weber, PhD, leads a team of Advisory Panel members who are working with ADDF-Harrington Scholar Travis Dunckley, PhD, to translate his discovery into a drug. Here, Dr. Weber describes the milestones they have achieved to date.

1. Dr. Weber and Advisory Panel colleagues reviewed Dr. Dunckley’s drug discovery research and recommended additional laboratory studies to determine the exact quantities of inhibitors that are present in the brain during his studies using animal models of Alzheimer’s disease (AD).

2. Dr. Dunckley completed a study with three different inhibitors as recommended by his Advisory Panel mentors. Consistent with Dr. Dunckley’s results showing improved learning in the animal models, the molecules did reach the brain, although higher brain levels are needed for a drug molecule.

3. Development of an intellectual property (IP) portfolio is a major milestone that will help shape the drug’s future. With input from Harrington Discovery Institute’s legal counsel, Dr. Dunckley, his collaborators and their attorneys are hammering out the details of a patent application to be clear, strong and attractive to investors.

Now, with the initial pharmacokinetics study completed and plans in place for improving the levels and residence times of inhibitors in the brain, Dr. Weber and her Advisory Panel colleagues will take a step back to examine Dr. Dunckley’s project more broadly.

“Dr. Dunckley has something unique – the first kinase inhibitor potentially able to reduce both types of protein aggregates, the intracellular tangles and extracellular plaques – that are the hallmarks of AD,” Dr. Weber notes. “We have been encouraging him to use his understanding of the kinase and its role in AD to identify what other pieces of data he might need to improve preclinical tests. These, along with more potent molecules, will make his approach of greater interest to investors.”

Dr. Weber is also a member of the Department of Chemistry and Biochemistry Advisory Board at the University of Arizona, Tucson, where she is a mentor in the Careers in Chemical Sciences Program.

Innovation Support Center Advisory Panel Member: Patricia C. Weber, PhD

Patricia C. Weber, PhD, has spent more than 30 years in the pharmaceutical industry, first with some of the biggest players in the business and since 2002 as an entrepreneur with biotechnology start-ups. A graduate of the University of Arizona with a PhD in chemistry, Dr. Weber conducted her postdoctoral research at Yale University, studying DNA-binding proteins with 2009 Chemistry Nobel Laureate Thomas Steitz, PhD.

She launched her career in commercial biotechnology and drug discovery as a research scientist in the DuPont Central Research and Development Department, rising to the position of Associate Director of DuPont Pharmaceuticals in 1991. In 1994, Dr. Weber left DuPont to become Senior Director, Structural Chemistry at Schering-Plough Research Institute. In that position she supervised several interdisciplinary teams, contributing to multiple drug development programs that produced new drug candidates.

In 2002, Dr. Weber turned her focus to venture-backed and government-funded technology start-ups. She works with both academic and industrial entrepreneurs. Dr. Weber has been a member of the Innovation Support Center Advisory Panel since 2016, applying her management, business and technical experience in drug discovery and development to mentor Harrington Scholars.
Setting Ambitious Goals

Oxford-Harrington Scholar Valentine Macaulay, MD, PhD, FRCP, has an “extremely interesting” project underway, according to drug development veteran George Trainor, PhD. As a member of the Harrington Discovery Institute’s Innovation Support Center Advisory Panel, Dr. Trainor is advising Dr. Macaulay in her scientific work. The duo has set specific and ambitious goals to achieve over the next two years, the duration of Dr. Macaulay’s Oxford-Harrington award.

Dr. Macaulay has developed a therapeutic hypothesis based on the observation that people with rare genetic disorders that suppress insulin-like growth factor (IGF) signaling are nearly completely protected from cancer. The key milestone will be establishing proof of concept for a new way to block IGF signaling in cancer cells.

For the first three months of the award, Dr. Trainor met with Dr. Macaulay several times in person to assist her in setting up an extremely sophisticated screening technology. “At this early stage, she is looking to screen available small molecules to identify those that block the IGF signaling in cancer cells,” Dr. Trainor says.

The results of the screening will be foundational to Dr. Macaulay’s next steps. When the screening is complete, Dr. Trainor will advise Dr. Macaulay on the synthesis of drug candidates based on the most effective molecules. Ultimately, this process will identify the small molecules with the highest potential to be developed into drugs.

Dr. Macaulay is still in the preliminary phases of drug discovery, but Dr. Trainor expects this program will be able to move quickly once the initial screening is complete. “Oxford University is exceptionally strong in basic medical research and is developing in its drug discovery capability,” he notes. “The interaction with the Harrington Discovery Institute’s Innovation Support Center will accelerate this development.”

“Impressed and inspired”

In 2015, Dr. Trainor and his wife formed Trainor Consulting, offering consultation on all aspects of drug discovery. As a member of the Innovation Support Center Advisory Panel since 2012, Dr. Trainor advises Harrington Scholars on a wide range of issues, including medicinal chemistry and drug discovery strategy.

“Everyone in drug discovery dreams of getting to this place and works for years to get there. Knowing we are one the verge of being in the clinic is incredible.”

Jerri Rook, PhD
2015 ADDF-Harrington Scholar

Innovation Support Center Advisory Panel Member: George Trainor, PhD

George Trainor, PhD, brings more than 30 years of drug discovery and development experience to Harrington Scholars and the Innovation Support Center.

A graduate of Harvard University with a PhD in chemistry, he completed postdoctoral work at Columbia University before joining the Research and Development department at DuPont. During his tenure there, Dr. Trainor invented the most commonly used genetic sequencing technology, a tool to determine the sequence of the four nucleotides that make up DNA.

He rose to the position of Executive Director for Medicinal Chemistry at Dupont/Dupont Merck Pharmaceuticals, responsible for drug discovery strategy and execution. In 2001, DuPont Pharmaceuticals merged with Bristol Myers Squibb Company where he was appointed Vice President of Oncology and Early Discovery Chemistry. In this position he led medicinal chemistry efforts for oncology drug discovery and hits-to-leads activity for all therapeutic areas. His scientific teams advanced more than three dozen drug candidates into development.

In 2011, Dr. Trainor and his wife formed Trainor Consulting, offering consultation on all aspects of drug discovery. As a member of the Innovation Support Center Advisory Panel since 2012, Dr. Trainor advises Harrington Scholars on a wide range of issues, including medicinal chemistry and drug discovery strategy.
Achieving a Major Milestone

2015 ADDF-Harrington Scholar Jerri Rook, PhD, Assistant Professor, Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, Tenn., is preparing to launch a clinical trial of a new drug therapy to improve memory in Alzheimer’s disease patients. She has worked closely with Peter Bernstein, PhD, Innovation Support Center Advisory Panel member, to prepare for a Phase 1 clinical trial.

“Jonathan (Stamler) is a visionary,” Dr. Rook says. “The resources he put together - a team of drug discovery scientists with decades of experience - have never been available to academia in the past.”

Dr. Rook applied to the Harrington Discovery Institute on the recommendation from ADDF, which provided the initial grant for her work in 2014. With the ADDF’s resources, Dr. Rook and the Vanderbilt Center for Neuroscience Drug Discovery team had advanced their drug candidate through preclinical trials that demonstrated efficacy.

Since 2015, Dr. Bernstein and his Innovation Support Center colleagues have guided her through the many studies required for filing an Investigational New Drug (IND) application. “There are a million pitfalls along the way in drug development, and the process requires a whole new set of expertise,” Dr. Rook explains. “The incredible people of the Innovation Support Center offered us a wealth of knowledge that has got us to this point.”

Dr. Bernstein believes the mentoring process works so well because the Harrington Scholars and Innovation Support Center experts work together as equal teammates. “Every member of the team brings their expertise to the project to develop strategies,” he explains. “We share a common goal of developing a new drug that is both meaningful and competitive in the market.”

“The Harrington Scholars’ scientific knowledge and familiarity with their individual projects complements the Innovation Support Center members’ sixth sense,” Dr. Bernstein adds. “Our Advisory Panel members know what has a chance for success, gained from their personal experience with overcoming or recovering from approaches and projects that failed.”

Innovation Support Center Advisory Panel Member: Peter R. Bernstein, PhD

Peter R. Bernstein, PhD, has devoted his career to transforming basic science into successful clinical research that results in drug discovery and development. A recognized expert in medicinal chemistry, Dr. Bernstein enjoyed a 30+ year career as a scientist with AstraZeneca Pharmaceuticals, rising to the senior level of the AstraZeneca scientific ladder and developing expertise across multiple therapeutic areas.

He retired from AstraZeneca in 2010 to establish his own consulting firm, providing guidance on small molecule drug discovery and development with a focus on the neuroscience and inflammatory disease areas.

Dr. Bernstein earned his bachelor’s degree in chemistry from the University of Rochester, magna cum laude, and his PhD in organic chemistry from Columbia University. He conducted postdoctoral research at the University of Wisconsin, designing and delivering a total synthesis of vitamin D.

Dr. Bernstein has more than 150 published scientific papers and presentations to his credit and is a frequent guest lecturer and instructor at meetings and universities around the world. He is an inventor on more than 60 patents related to drug discovery. Dr. Bernstein has received numerous honors during his career, including Distinguished Lecturer for the 2010 AstraZeneca Excellence in Chemistry Awards, election to the American Chemical Society Division of Medicinal Chemistry Hall of Fame in 2011, and Distinguished Guest Professor, Tübingen Universität 2016.
In the five years since its founding, BioMotiv, the for-profit drug accelerator of The Harrington Project for Discovery & Development, has catapulted from start-up mode to scale-up mode.

With single-minded purpose and inspiration from the entrepreneurial attitude of The Harrington Project founder Ron Harrington, BioMotiv licenses discoveries and develops them into promising new drugs that are advanced through the stages of pre-clinical development before applying for approval for testing in humans. The accelerator aims to produce a portfolio of breakthrough medicines that are advanced into clinical trials.

“We have a unique system – Harrington Discovery Institute, the Innovation Support Center, disease foundation partners, and strategic investment, development, and pharmaceutical partners – all complementary resources and capabilities, mission-aligned to bring new medicines to market,” says BioMotiv CEO Baiju R. Shah.

Investors have embraced the concept, supporting BioMotiv with $145 million in total funding from strategic partners, institutional investors and family offices. “Our business model is focused on delivering all the essential elements to efficiently de-risk, advance and partner innovative drugs at the early stages of development,” Shah explains.

He believes BioMotiv is poised to expand over the next five years. “We have built a solid foundation, including the structure, processes, partnerships and culture, to enable success. Our focus now is on rapidly broadening our portfolio and accelerating multiple new medicines into the clinic,” he notes.

Beyond its investments in discoveries from Harrington Scholars, BioMotiv also funds promising discoveries from academic institutions across the country and around the world, including new opportunities in the past year from the University of Auckland, New Zealand and the University of Michigan.
BioMotiv’s Mission and Milestones

BioMotiv has supported 11 companies and projects since its inception. Here are snapshots of several companies based on discoveries from Harrington Scholars. Each one represents a milestone in fulfilling BioMotiv’s mission: Accelerating Breakthrough Discoveries into Medicines.

**OptiKira**

BioMotiv established OptiKira in 2015 to advance discoveries made by University of California, San Francisco physician-scientists and 2013 Harrington Discovery Institute Scholar-Innovators Feroz Papa, MD, PhD, and Scott Oakes, MD, and their colleagues at UCSF and the University of Washington. Their work targeted a biologic pathway leading to progressive cell death in a variety of diseases, including retinitis pigmentosa (RP), diabetes and amyotrophic lateral sclerosis (ALS). OptiKira is engaged in development of a drug to inhibit this pathway in RP to prevent death of photoreceptors, the cells in the eye necessary for vision, and prevent blindness. The company is also developing drugs based on the original discovery that can be used systemically for the treatment of ALS. Since launching, the company has received additional investment support from Arix Bioscience (a BioMotiv strategic partner) and has been awarded numerous grants to advance its technologies.

**Allinaire**

Launched in 2016, Allinaire is focused on developing new treatments for chronic obstructive pulmonary disease (COPD) and other lung diseases. Allinaire is advancing the discoveries made by 2014 Harrington Scholar-Innovator Irina Petrache, MD, of National Jewish Health, Denver, Colo., and her colleague Matthias Clauss, PhD, Indiana University School of Medicine, Indianapolis, Ind. They identified a target in a biologic pathway that is central in the destruction and death of lung tissue in COPD and found an antibody that acts against this target to slow disease progression. Allinaire is progressing this antibody towards commercialization, supported by BioMotiv, Indiana investment funds and federal commercialization grants.

**Sujana**

BioMotiv founded Sujana in 2015 to develop new treatments for inflammatory and blood vessel disorders. Harrington Distinguished Scholar Daniel I. Simon, MD, University Hospitals, Cleveland, and colleagues from Cleveland Clinic and Case Western Reserve University have identified the workings of a cellular mechanism that attracts and activates leukocytes, a type of immune cell, at sites of blood vessel injury. Sujana is developing a compound to inhibit this mechanism, which would prevent the inflammation that characterizes various disorders such as thrombosis, vasculitis, and multiple sclerosis. Sujana has received NIH commercialization grants to support its technology.
Harrington Discovery Institute and Takeda Pharmaceuticals Company Limited recently announced a collaboration to create the Harrington Rare Disease Scholar Award Program. The program will leverage the combined strengths, expertise and resources of the partners to advance breakthrough research for cures and meaningful treatment options for rare diseases.

Harrington Discovery Institute and Takeda JOIN FORCES

This collaboration is intended to be a step toward removing barriers between the academic community and the pharmaceutical industry while building upon the partners’ shared vision and mission of delivering innovative healthcare solutions for patients.

The Harrington Discovery Institute will select up to 10 researchers to receive the Harrington Rare Disease Scholar Award. In addition to funding support, scholars will work closely with drug development experts from the Innovation Support Center, which provides hands-on industry guidance not found in traditional academic research settings. Scholars will also have facilitated access to Takeda experts and resources to further assist them from the bench to the clinic.

The program will rely on Harrington Discovery Institute’s proven model, established networks, and experience working with academic researchers to maximize the clinical and commercial potential of selected projects.

Award recipients will be selected by Harrington Discovery Institute’s Rare Disease Scientific Advisory Council and announced in early 2018.

RARE DISEASES IN THE UNITED STATES

• The National Institutes of Health (NIH) defines a disease as rare if it has a prevalence of fewer than 200,000 affected individuals in the United States.

• 1 in 10 Americans has a rare disease. This adds up to 30 million people with a serious lifelong disease.

• 80% of rare diseases are genetically based.

• Medications and other products developed to diagnose, prevent or treat rare diseases are called orphan drugs.

• There are 500 approved orphan drugs.

• Only 5% of rare diseases have a treatment available.

Source: National Organization for Rare Disorders
Impact Philanthropy
FROM THE HEART

How two heartfelt gifts will make a difference in the future

Harvey and Ruth Nevins and Larry and Debbie Harlan have never met. The Nevins live in Willoughby, Ohio; the Harlans live in Scottsdale, Ariz. Mr. Nevins is a retired businessman; Dr. Harlan is a retired dentist.

As different as they are in some ways, the two couples share a common desire to help turn breakthrough discoveries into life-changing, life-saving medicines. That deep desire has inspired both couples to establish funds with Harrington Discovery Institute, earmarked for support of Harrington Scholars who are researching specific diseases.

A Selfless Gift

The Nevins are passionate about diabetes research. Diagnosed with Type 2 diabetes some 20 years ago, Mr. Nevins is now experiencing the disease’s long-term debilitating effects, including serious damage to his kidneys. In March 2017 he began dialysis three days a week. “Diabetes is a terrible disease,” Mr. Nevins says. “We hope someone can find a cure through research so that people will not have to suffer like I have. That is my dream.”

Mr. and Mrs. Nevins established the Ruth C. and Harvey I. Nevins Diabetes Acceleration Fund at Harrington Discovery Institute through an estate plan in 2016. They shared their plan with their two daughters and worked with an attorney to ensure their fund was set up in a way that would ensure their gift could accomplish the greatest good. “It has turned out exactly as I wanted,” Mr. Nevins says with satisfaction.

A Hopeful Tribute

The Harlan’s fund is focused on macular degeneration research. “My mother had the dry form of (age-related) macular degeneration (AMD), for which there is no cure, and it affected her life in such negative ways,” Mrs. Harlan recalls.

When her mother, Marjorie Bach, was diagnosed with AMD in her 60’s, Mrs. Harlan watched her slowly lose her vision. It was a sad progression as her mother, a lifelong avid reader, became unable to enjoy reading. Eventually, as the disease robbed her of many interests, she lost her will to live.

Mrs. Harlan is very much aware of the genetic component to AMD, and that played into her decision to establish an AMD research fund. “For my mother and for me, I thought it would be worthwhile to do this in her honor and memory,” she says. Dr. Harlan supported his wife’s wishes, and the couple established the Bach Family Foundation Acceleration Fund for Innovation at Harrington Discovery Institute to support a Harrington Scholar conducting research in AMD.

Mrs. Harlan’s intent is as clear as the Nevins’. “I would like to see someone come up with a cure or a treatment to slow AMD’s progression,” she says. “Research is the key. It has to start somewhere.”

Through their generosity and selflessness, the Nevins and the Harlans have become an enduring part of Harrington Discovery Institute’s mission.
World leaders in medicine, science and academia assembled in Cleveland to attend the Fifth Annual Harrington Scientific Symposium on May 23 and 24, 2017 and mark the significant milestones Harrington Discovery Institute has achieved in its first five years. In the words of Harrington Discovery Institute President Jonathan S. Stamler, MD, “In 2012, the new drug development model we designed began to attract the notice of investigators, investors and the pharmaceutical industry. Now, five years later, they are taking notice of our accomplishments.”

In a brief but inspiring presentation, Harrington Project founder Ronald G. Harrington expressed his and his family’s vision for The Project’s future. He referred to the significant financial support The Harrington Project has attracted – currently $330 million – as a means to an end, bringing new medicines to the clinic. Speaking from the heart, Mr. Harrington quoted one of his favorite proverbs, which embodies his reasons for founding The Harrington Project, “Society grows great when old men plant trees whose shade they know they shall never sit in.”

1985 Nobel Prize laureate Joseph L. Goldstein, MD, delivered the keynote address. Dr. Goldstein and his colleague Michael S. Brown, MD, won the prize for their discovery of the low-density lipoprotein (LDL) receptor and determining how it controlled cholesterol homeostasis. Dr. Goldstein, who is Professor and Chairman, Department of Molecular Genetics UT Southwestern Medical Center; Julie and Louis Beecherl Jr. Distinguished Chair in Biomedical Research and Regental Professor of the University of Texas, referred to Harrington Discovery Institute as “a really impressive endeavor that is unlike any other that I have heard of.”

In addition to Dr. Goldstein, the Harrington Symposium was honored to have FDA Commissioner 2016-2017, Robert M. Califf, MD, MACC, provide inspirational remarks during the five year anniversary celebration and dinner. Other presenters at the symposium included Andrew I. Schafer, MD, Weill Cornell Medical College, and Roger Stein, PhD, Financial Engineer, MIT Sloan School of Management.

Many leaders of American medicine were in attendance, including members of the Harrington Scientific Advisory Board, David Ginsburg, MD, William G. Kaelin, Jr., MD, Solomon H. Snyder, MD, DSc, DPhil, Andrew R. Marks, MD and Michael Welsh, MD, as well as, Daniel J. Drucker, MD, and Joel F. Habener, MD, who shared the 2017 Harrington Prize for Innovation in Medicine for their discovery of incretin hormones and their subsequent development of breakthrough therapies for diabetes with Jens J. Holst, MD, DMSc, who was unable to attend the symposium.

As tangible evidence of the milestones Harrington Discovery Institute has achieved since 2012, two Harrington Scholars presented about their experiences as recipients of Harrington awards. 2015 Harrington Scholar-Innovator Marikki Laiho, MD, PhD, Johns Hopkins School of Medicine, described the progress she has made in two years with a potential cancer drug targeting the RNA polymerase I pathway. She credited the Harrington Innovation Support Center for “bringing in really great experts in the areas where we have needed them” to advance her lead compound to preclinical trials.
Likewise, for Jerri Rook, PhD, Vanderbilt University and a 2015 ADF-Harrington Scholar, the Harrington Innovation Support Center has played a pivotal role in advancing her drug. She and her team discovered and are developing a new drug therapy to improve memory in Alzheimer’s disease patients and are preparing to enroll patients in a Phase I clinical trial beginning in the summer of 2017.

“Through the help of the ISC (Innovation Support Center), in two short years we have been able to navigate the IND (Investigational New Drug) process,” Dr. Rook stated. “Without the generosity of the Harrington family and this unprecedented model, we would not be going into this trial.”

“It was the most enjoyable conference I have ever attended - the depth and breadth of the speakers and the other participants was incredibly impressive. I am not sure that I have personally seen so many HHMI investigators assembled in one place.”

David B. Lombard, MD, PHD
2017 Harrington Scholar-Innovator
HARRINGTON SCHOLARS

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
The University of Texas 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 in St. Louis

2016 Harrington Scholar-Innovators

Nunzio Bottini, MD, PhD
University of California, San Diego

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
Weill Cornell Medical College

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

Gavril W. Pasternak, MD, PhD
Memorial Sloan-Kettering Cancer Center

Irina Petrache, MD
National Jewish Health

David H. Rowitch, MD, PhD
University of California, San Francisco

Jean Y. Tang, MD, PhD
Stanford University

David Wald, MD, PhD
Case Western Reserve University
2013 Harrington Scholar-Innovators
Marc I. Diamond, MD
UT Southwestern Medical Center
Roger A. Greenberg, MD, PhD
University of Pennsylvania
Geoffrey C. Gurtner, MD, FACS
Stanford University
Richard N. Kitsis, MD
Albert Einstein College of Medicine
Wolfgang B. Liedtke, MD, PhD
Duke University
Sanford D. Markowitz, MD, PhD
Case Western Reserve University
Scott A. Oakes, MD
University of California, San Francisco
Feroz R. Papa, MD, PhD
University of California, San Francisco
Jonathan D. Powell, MD, PhD
The Johns Hopkins University
Larry S. Schlesinger, MD
The Ohio State University
Robert B. Wilson, MD, PhD
University of Pennsylvania

2016 Alzheimer’s Drug Discovery Foundation-Harrington Scholars
Travis L. Dunckley, PhD
Arizona State University
Sung Ok Yoon, PhD
The Ohio State University

2015 Alzheimer’s Drug Discovery Foundation-Harrington Scholars
Carol A. Colton, PhD
Duke University
Jerri M. Rook, PhD
Vanderbilt University

2014 Alzheimer’s Drug Discovery Foundation-Harrington Scholars
Thota Ganesh, PhD
Emory University
Chien-Liang Lin, PhD
The Ohio State University

2017 Gund-Harrington Scholars
Shannon E. Boye, PhD
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
University of Oxford
Claudia Monaco, MD, PhD
University of Oxford

2014 Oxford-Harrington Scholar
Alison Simmons, MD, PhD
University of Oxford

For more information visit HarringtonDiscovery.org/Scholars