

# FIRST TEN YEARS

ACCELERATING DISCOVERIES INTO MEDICINES  
HARRINGTON DISCOVERY INSTITUTE 2012 – 2022



**Harrington Discovery Institute**



University Hospitals | Cleveland, Ohio

*Thank you*  
**VISIONARIES, EARLY BELIEVERS,  
ADVISORS AND TEAM MEMBERS**





*Thank you* **HARRINGTON SCHOLARS**



**WE CURE DISEASES** *together!*





**JONATHAN S. STABLER, MD**

President and Co-Founder, Harrington Discovery Institute  
Robert S. and Sylvia K. Reitman Family Foundation Distinguished Professor  
of Cardiovascular Innovation and Professor of Medicine and of Biochemistry at University Hospitals  
and Case Western Reserve University School of Medicine

# DEAR COLLEAGUES,

In 2022, we transitioned from a “mostly COVID-19” to a “post-COVID-19” world. We resumed work on the programs we had, in essence, shut down. The people of Harrington Discovery Institute found tremendous satisfaction in reprising the complex task of advancing our portfolio of 177 medicines in the making (and 36 companies launched, 19 medicines in the clinic and 13 licenses to pharma). Medical discovery is extraordinarily exciting at this moment in time, with once-in-a-century platforms, including gene editing and nucleic acid-based therapies, opening up whole frontiers for new treatments and cures.

We regained momentum in our flagship Scholar-Innovator program. Supporting physician-scientists with the resources they need to place their breakthrough discoveries on the right pathway in the drug development ecosystem is a founding principle of Harrington Discovery Institute. Our annual scientific symposium, a virtual event in 2022, went very well in this respect. We are continually amazed at the strength of scholars and projects from 64 major academic medical institutions throughout the US, Canada, and the UK.

We built ever-greater strength into our centers for major diseases, brain health medicines, rare diseases, and COVID-19. Our team of experienced therapeutics development experts gave their best every day in partnering with physicians and scientists in order to determine therapeutic targets and regulatory pathways, assess commercial viability, and more. We are proud that our centers, advisors, scholars, and innovators made big progress in advancing scientific breakthroughs and finding novel medicines for unmet need.

We worked to restore a personal touch to our organization. During COVID, we, like so many organizations, urgently replaced the personal feel we prized with an impersonal set of protocols. We felt the loss of face-to-face, normal (unhurried, thoughtful) interactions at every level. Just as breakthrough science happens sometimes through random intersections, so too does organizational personality and warmth. I feel we have not succeeded in restoring this sense to the organization—yet.

Impact philanthropy and impact investments continued to be dynamic, evolving sources of funds. Many impact philanthropists have great desire for meaningful sustained improvements in medicine, as do impact investors, such that contemporary non-profits like ours must become acquainted with many shapes and sizes of monies.

In 2023, I am eager for us to try new things that add even more warmth, culture, and a deep sense of belonging to our organization. In parallel, we have set the goal in 2023 of continuing to build out our foundation of impact philanthropy. We want to ensure that all people blessed with financial means understand that the way to move medicine into new frontiers for patients is to lean into generosity, creativity, and impact.

Sincerely,



# TABLE OF CONTENTS

## 2-3

A letter from

**Jonathan S. Stamler, MD**

President, Harrington Discovery Institute

## 6-7

Our Impact

## 8

The Ripple Effects of Philanthropy

**Ronald G. Harrington**

Philanthropist and Entrepreneur

## 9

Multiple Paths to Support

One Mission

## 10-11

Oxford-Harrington

Rare Disease Centre

**Matthew Wood**, Professor of  
Neuroscience, University of Oxford

**Diana Wetmore, PhD**, Vice President  
of Therapeutics Development,  
Harrington Discovery Institute

## 12-13

Unlocking the Potential of Human  
Antibodies to Fight COVID-19

**James Crowe, MD** and  
**Michel Nussenzweig, MD, PhD**  
2022 Harrington Prize Recipients

## 14-15

A Breakthrough Platform For  
A Multitude of Discoveries

**Jonathan S. Stamler, MD**  
Harrington Investigator

## 16-17

Harrington Scholar Programs

## 18

Congratulations New Scholars

## 19

Meet Our 2021 and 2022  
Harrington Scholars

## MAJOR DISEASES

Physician-Scientist Initiative

**20** Harrington Impact

## 2021 HARRINGTON SCHOLAR-INNOVATORS

**21** Jennifer Chen, MD

**22** John Chorba, MD

**23** Joseph Contessa, MD, PhD

**24** Toren Finkel, MD, PhD

**25** Aaron Schimmer, MD

**26** Jill Smith, MD

**27** Xinnan Wang, MD, PhD

## 2022 HARRINGTON SCHOLAR-INNOVATORS

**28** Burton Dickey, MD

**29** Diana Farmer, MD

**30** James Hagood, MD

**31** Li Lan, MD, PhD

**32** Carolyn Lee, MD, PhD

**33** Michael Lin, MD, PhD

**34** Francis McCormack, MD

**35** David Myung, MD

**36** Bernd Schnabl, MD

**37** Loren Walensky, MD, PhD

**38** Hans-Guido Wendel, MD

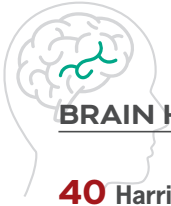
## 2021 HARRINGTON-MSTP SCHOLAR

**39** Derek Wong

## OUR INNOVATION CENTERS



FOR MORE INFORMATION:  
[HarringtonDiscovery.org/Centers](https://HarringtonDiscovery.org/Centers)



## **BRAIN HEALTH MEDICINES**

**40** Harrington Impact

**2021 ADDF-HARRINGTON SCHOLAR**

**41** Christiane Wrann, DVM, PhD

**2022 VINNEY SCHOLARS**

**42** Nabil Alkayed, MD, PhD

**43** Xin Qi, PhD



## **RARE DISEASES**

**44** Harrington Impact

Our rare disease scholars have been profiled in past annual publications.

For more information, visit:

[HarringtonDiscovery.org/UK-Rare-Disease](https://HarringtonDiscovery.org/UK-Rare-Disease) and

[HarringtonDiscovery.org/US-Rare-Disease](https://HarringtonDiscovery.org/US-Rare-Disease).



## **COVID-19**

**45** Harrington Impact

Our COVID-19 scholars have been profiled in past annual publications.

For more information, visit:

[HarringtonDiscovery.org/HarringtonCoronavirus](https://HarringtonDiscovery.org/HarringtonCoronavirus).

**46-47**

**The Harrington Advantage: Relationships Are In Our DNA**

Diana Wetmore, PhD

**48-49**

**Case Study: A Two-Time Harrington Scholar's Path to Developing a Mitochondrial Medicine**

Xin Qi, PhD

2018 Harrington Rare Disease Scholar

2022 Vinney Scholar

**50-51**

**Case Study: Taking Precise Aim at Rheumatoid Arthritis**

Nunzio Bottini, MD, PhD

2016 Harrington Scholar-Innovator

**52-53**

**Major Gift Spotlight: Challenging the Status Quo in the Fight Against Alzheimer's Disease**

Cathy and Paul Douglas

Philanthropists

**Dementia: The Great Unmet Need of Our Time**

Andrew Pieper, MD, PhD

Director, Center for

Brain Health Medicines

Harrington Discovery Institute

**54-55**

2022 Scientific Symposium

**56-59**

Harrington Scholars 2013-2023

# 10 YEARS

*thank you*

**DISCOVERY AND FUNDING PARTNERS**

**HARRINGTON TEAM**

**IMPACT PHILANTHROPISTS**

**INVESTMENT ADVISORY BOARD**

**SCIENTIFIC ADVISORY BOARD**

**THERAPEUTICS DEVELOPMENT CENTER ADVISORS**

## SUCCESS METRICS

**177** MEDICINES IN  
THE MAKING

**64** INSTITUTIONS  
SUPPORTED

**36** COMPANIES  
LAUNCHED

**19** MEDICINES  
IN THE CLINIC

**13** LICENSES  
TO PHARMA



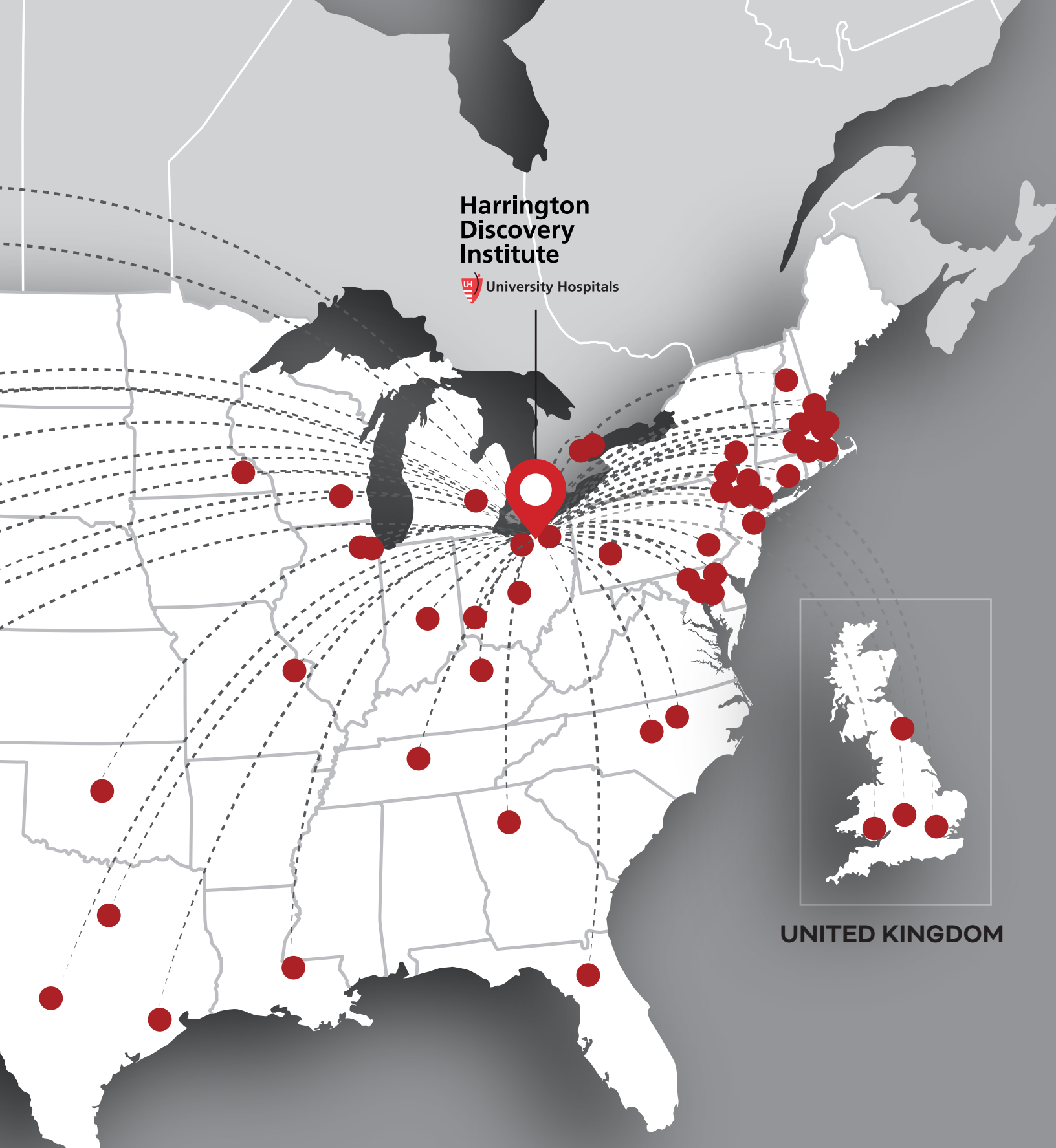
# OUR IMPACT

HARRINGTON SCHOLAR PROJECTS SUPPORTED



# Harrington Discovery Institute

 University Hospitals



**UNITED KINGDOM**



FOR MORE INFORMATION:  
[HarringtonDiscovery.org/Impact](http://HarringtonDiscovery.org/Impact)



*“It’s hard to believe the impact a gift can have when you invest in the right people, the spark it can create. Harrington Discovery Institute is a home for innovators and there is so much more we can accomplish together.”*

**RONALD G. HARRINGTON**  
Philanthropist and Entrepreneur

## THE RIPPLE EFFECTS OF **PHILANTHROPY**

Harrington Discovery Institute started with one family’s philanthropic investment, and the cascading impact of that decision is still felt a decade later. Today, Harrington Discovery Institute has global reach and a track record of developing new treatments and cures, with over 177 medicines in the making, 36 companies launched, and 19 medicines in the clinic. By offering their time, insight, and philanthropy, the Harrington family started a chain of events that is bringing together world-class scientists, developers, investors, families, and donors and fundamentally altering the landscape for drug discovery.

“Ten years ago, my family and Dr. Jonathan Stamler decided we wanted to do something about diseases without cures, and to shake up the traditional thinking about drug development,” said

Mr. Harrington. “We threw a rock into a very large pond and it’s amazing to see everything that’s happened since then. I’m not a scientist, so I’m humbled when I see the world-class physician-scientists whose potential has been unleashed because of this institution. When I hear from families who are fighting alongside us to develop new treatments, we can’t help but think about where we started. It’s hard to imagine the impact one family can have when you invest in the right people with the right ideas.”

Emerging partnerships with philanthropists in Canada, Mexico, and the UK have Mr. Harrington energized while still conscious of how much it takes to advance this work. “A lot of people talk about innovation in healthcare, but we have a model that is truly disruptive and scalable. Few things

are more gratifying than speaking to a new donor to Harrington Discovery Institute—there’s just so much excitement when you realize the effect you and your family will have on people’s lives. The pond is still very large but, together, our ripples are becoming a wave,” he adds.

Lastly, Mr. Harrington offered a word of caution for philanthropic families seeking to make a difference. “The ideas don’t mean anything unless you have trust in the leadership and culture of the institution. Dr. Jonathan Stamler is uniquely qualified to lead this, and he has surrounded himself with some of the most impressive scientists and team members imaginable. For philanthropists, Harrington Discovery Institute is a low-risk investment with an immensely high potential for reward.”

# MULTIPLE PATHS TO SUPPORT ONE MISSION

## Impact Philanthropy

Morgan Stanley GIFT Cures<sup>SM</sup> powered by Harrington Discovery Institute was established as the first special interest program of Morgan Stanley Global Impact Funding Trust (GIFT) in response to client demands for concrete results from their medical philanthropy.

As patients and their families look to make an impact through their charitable donations, the field of global philanthropy in particular has played a large role in advancing medical discoveries. Most recently, Morgan Stanley GIFT Cures received a major donation in memory of an individual who cared deeply about increasing treatment options for patients battling cancer. The gift will benefit Harrington Discovery Institute's mission and specifically lung and pancreatic cancer-focused initiatives.

## Impact Investing

Harrington Discovery Institute has established three investment vehicles to commercialize technologies. Each is closely aligned with the Harrington mission of advancing new medicines in areas of unmet need and has its own objectives and policies. To date there have been several dozen investments in new treatments for diseases ranging from cancer to metabolic diseases, infectious diseases, diabetes, neurological disorders, and rare diseases.

- **Advent-Harrington Impact Fund** is a joint effort with leading venture fund manager Advent Life Sciences, to invest in promising drug discovery assets, including projects generated by Harrington scholars.
- **BioMotiv** is a mission-driven investment fund to translate Harrington breakthrough discoveries into novel medicines through alignment with the right investors and commercialization partners.
- **Harrington Discovery Institute Seed Fund** is an internal investment fund that enables early investments in scholar projects, as well as mission-aligned projects outside the Harrington community.







# Oxford-Harrington RARE DISEASE CENTRE

## TRANSATLANTIC PARTNERSHIP

The Oxford-Harrington Rare Disease Centre (OHC) is a unique partnership between the University of Oxford and Harrington Discovery Institute that combines world-class strengths in research and therapeutics development. With the aim of delivering new medicines for patients suffering from rare diseases, it is on the front wave of rare disease drug discovery and development.

The OHC is gaining international recognition for its tremendous research and commercialization capabilities as well as its big goals. It plans to support over 50 rare disease drug projects, and advance 20 new medicines into the clinic, within 10 years.

## PRIORITIES

The OHC prioritizes diseases:

- That affect mainly children
- Where the treatment may impact adult diseases
- That fill an urgent need with great impact, and
- That fall in the areas of rare neurological diseases, cancers, and developmental diseases.

## CLINICAL TRIALS

Clinical trials are a vital stop on the journey of drug development. The OHC is uniquely positioned to accelerate the testing of new medicines in clinical trials. With a very rare disease, there may be a small pool of affected people across the US and Europe. The OHC transatlantic network can help identify patients for clinical trials. “We can build networks of clinical trials across multiple

projects from the UK, US, and Canada,” said Professor Matthew Wood, a neuroscience professor at Oxford and director of the OHC.

## COLLECTIVELY COMMON AND COSTLY

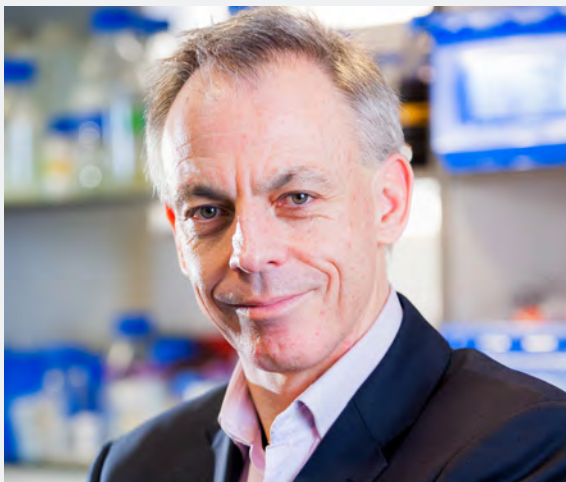
Rare diseases are individually rare but collectively common. They affect at any point in time 3.5% - 5.9% of the worldwide population, which equates to approximately 300 million people. Despite the prevalence of rare diseases, it is often a very difficult and time-consuming road to get to a correct diagnosis, let alone an effective treatment—if one exists.

“It is incredibly burdensome to society in economic and psychological terms,” said Prof. Wood.

Then, too, there are the economic costs of untreated rare diseases to families and society—likely hundreds of billions of dollars.

Meanwhile, the cost for finding new treatments and cures is decreasing. Gene therapy and editing cost less than traditional drug discovery and development, and are expected to lower the cost of developing new drugs for rare diseases.

Diana Wetmore, PhD, Vice President of Therapeutics Development at Harrington Discovery Institute, said, “We are at the beginning of an expansion of knowing which genetic mutations cause rare diseases. Now, people in drug discovery are working on platforms that could be used for many diseases.”



*“There are significant challenges in meeting the needs of rare diseases. With advances in genomics and drug delivery and development, we are now in a position to make a difference for people who have had little hope of finding a treatment.”*

**MATTHEW WOOD**

Professor of Neuroscience  
University of Oxford  
Director, Oxford-Harrington Rare Disease Centre

**RARE DISEASE SYMPOSIUM**

In September 2022, the OHC held its rare disease symposium at University of Oxford. This well-attended event featured terrific presentations made by international industry participants, researchers, and guests. The symposium focused particularly on neurology and cancer.

At one point, Prof. Wood was chairing a session of drug experts. A 2021 Harrington UK Rare Disease Scholar, Haiyan Zhou, MD, PhD of University College London, said so many positive things

about Harrington resources that Prof. Wood says he found himself blushing.

“I was trying to wrap up the panel discussion,” he recalls, “and she said, ‘Wait, I’m not finished yet,’ and complimented the many resources Harrington has brought to bear. Her words had huge impact because she is exactly who we at the OHC are trying to serve.”



FOR MORE INFORMATION:  
[HarringtonDiscovery.org/OHC](https://HarringtonDiscovery.org/OHC)



*“There is no greater impact a person could have on society from a health perspective than to help us address the huge gap between 7,000 rare diseases with no existing treatments today and having new drug interventions to help cure and treat people who need them.”*

**DIANA WETMORE, PhD**

Vice President, Therapeutics Development Center  
Harrington Discovery Institute



## UNLOCKING THE POTENTIAL OF HUMAN ANTIBODIES TO FIGHT COVID-19

The COVID-19 pandemic shone a spotlight on the groundbreaking work of Drs. Nussenzweig and Crowe. By uncovering fundamental principles of the human immune response, the researchers enabled the use of human antibodies to treat SARS-CoV-2, the virus that causes COVID-19. For their efforts, Drs. Nussenzweig and Crowe have been selected as co-recipients of the ninth annual Harrington Prize for Innovation in Medicine.

Dr. Nussenzweig addressed a critical issue in immunology—the lack of a detailed understanding of the human antibody response—by developing robust and scalable methods for cloning antibodies from single human B cells. He demonstrated that antibodies directly from humans can be a safe and effective treatment against viral infections when passively transferred to other humans. His work established a paradigm that made it possible to rapidly develop monoclonal antibody therapies against SARS-CoV-2.

Dr. Crowe advanced the discovery of human monoclonal antibodies for many of the most pathogenic viruses that

cause human disease. His team has discovered thousands of human monoclonal antibodies for SARS-CoV-2 and facilitated their development, transferring clinical leads to multiple pharmaceutical partners. His work on the genetic and structural basis of virus neutralization revealed important principles that are being applied in new vaccine and antibody development.

Dr. Nussenzweig's research focuses on the molecular aspects of the immune system's innate responses. His laboratory has isolated and cloned antibodies to the human immunodeficiency virus (HIV) and other viruses, and his research has led to the development of innovative vaccines and new treatments for autoimmunity.

Dr. Nussenzweig notes that vaccines are mediated by antibody responses. Some individuals infected with HIV develop serum antibody responses that are able to neutralize the virus. In clinical trials, Dr. Nussenzweig and his colleagues took the surface protein from HIV cells and used it to identify the B cell lymphocytes

in the serum of these individuals—in effect capturing the cells that were making very potent antibodies.

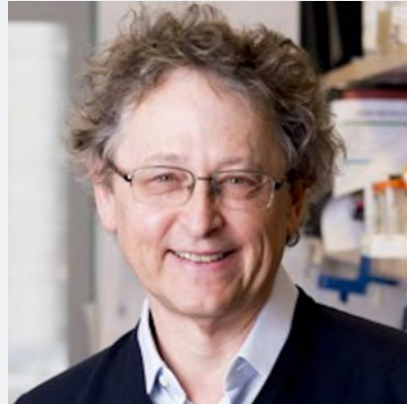
“This established that antibodies could be obtained directly from human B cell lymphocytes by tagging the B cells with the protein of interest,” Dr. Nussenzweig says.

He adds that, as natural human products, the antibodies produced are safe to administer to other humans and can be produced much faster than going through a traditional drug development process.

“We've developed a paradigm and a method for rapidly producing antibodies that can be used clinically,” Dr. Nussenzweig says. “They can be used for passive protection, chronic therapy and potential eradication of diseases.”

“I think that it would be wonderful if we could have a broad antibody for people who cannot respond to vaccines,” he adds. “One that the coronavirus cannot escape no matter how many mutations it makes.”





**(LEFT) JAMES CROWE, MD**  
 Director, Vanderbilt Vaccine Center and Professor,  
 Departments of Pediatrics and Pathology  
 Microbiology and Immunology  
 Vanderbilt School of Medicine

**(RIGHT) MICHEL NUSSENZWEIG, MD, PhD**  
 Investigator, Howard Hughes Medical Institute, and  
 Zarnil A. Cohn and Ralph M. Steinman Professor  
 The Rockefeller University

Dr. Crowe explains that his research into monoclonal antibodies is based on the finding that the human immune system has a long memory—and it holds grudges.

“Once you have encountered a foreign pathogen, the adaptive immune system—T cells and the antibody-producing B cells in your white blood cells—will remember the experience and will be prepared to defend against that pathogen if you encounter it again,” he says.

For example, Dr. Crowe and his team examined the blood of 100-year-old individuals and found circulating memory

B cells that still recognized the pathogen responsible for the global influenza pandemic of 1918-1919. Findings such as this led the team to believe that antibodies could be created for any infection for which they could find a survivor. In an experiment using a blood sample from a survivor of the 2014 Ebola virus outbreak in West Africa, Dr. Crowe and his team were able to sort out 15,000 new monoclonal antibody gene sets.

“We’re starting to get a deep view of the specificity and the genetics of the human immune system, and it’s vast,” Dr. Crowe says.

Dr. Crowe notes that although monoclonal antibodies are an amazing technology, they have been used predominantly for cancer and autoimmunity—they’re currently used very little for infectious diseases.

“COVID showed us that antibodies designed and used properly can have a major benefit for individuals who are at high risk,” he says. “I think we’re at a tipping point in medical history where we will now see antibodies and vaccines become equal partners in preventing infectious diseases.”



FOR MORE INFORMATION:  
[HarringtonDiscovery.org/Prize](http://HarringtonDiscovery.org/Prize)



**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.

A BREAKTHROUGH PLATFORM FOR

# A MULTITUDE OF DISCOVERIES

## A FUNDAMENTAL DISCOVERY

In addition to being president of Harrington Discovery Institute, Jonathan Stamler, MD, also is a Harrington Investigator with over 300 scientific papers and 223 patents. Most notably, he pioneered the field of Protein S-nitrosylation (SNO) in which basically all proteins are modified by SNO to regulate cellular function.

During his residency at Brigham and Women's Hospital, Dr. Stamler became interested in nitric oxide (NO). In 1992, he published a seminal paper outlining the discovery of SNO, which became a breakthrough platform for many discoveries. He found that proteins can be controlled by SNO modification, a fundamental process regulating essentially all classes of proteins in

physiology and also causing numerous diseases, from heart and lung diseases to neurodegeneration and cancer.

Dr. Stamler has a long track record of translating these fundamental discoveries into therapies that benefit humans. Early on he conceptualized that linking NO to other molecules would endow those molecules with NO bioactivity thereby creating new classes of drugs and materials with broad applications. More recently he has identified novel enzymes that control S-nitrosylation, opening the door to many therapeutic opportunities.

Exciting new developments in the Stamler lab include new treatments for heart disease, asthma and diabetes, and a wearable device to assess the health benefits of exercise.

## A CHOLESTEROL-LOWERING THERAPY

In 2022, Dr. Stamler and colleagues at Case Western Reserve University showed that a SNO-based treatment for lowering cholesterol levels could be developed.

The key to the new drug, which has been administered to patients in early studies, is that it inhibits the PCSK9 protein by attaching SNO. After statins, PCSK9 inhibitors are a leading class of medications for managing cholesterol. The Stamler lab found that this SNO-increasing drug could reduce PCSK9 levels to lower bad cholesterol by 70 percent.

With heart disease remaining the main cause of morbidity and mortality in the Western world, the discovery was exciting.

*“Cholesterol lowering is one of the most important therapies we have to prolong life and protect people from disease.”*



**JONATHAN S. STAMLER, MD**

President and Co-Founder, Harrington Discovery Institute  
Robert S. and Sylvia K. Reitman Family Foundation  
Distinguished Professor of Cardiovascular Innovation  
and Professor of Medicine and of Biochemistry at  
University Hospitals and Case Western Reserve  
University School of Medicine

“Cholesterol lowering is one of the most important therapies we have to prolong life and protect people from disease,” said Dr. Stamler. “Statins lower cholesterol only so far. We think this drug class is a new way to hit PCSK9 and lower cholesterol.”

**AN ASTHMA DRUG**

NO and SNO play a protective role during asthma attacks by opening airways, and activation of the  $\beta$ 2-adrenergic receptor, as by inhaler drugs, increases both. However, Dr. Stamler found that the receptor stops protecting against asthma when it is modified by SNO, and that mice with a mutated receptor that cannot be SNO-regulated do not develop asthma. This suggests that a drug that blocks SNO could be an important and useful therapy in asthma.

**A “WEARABLE” FOR BRAIN HEALTH**

SNO is carried by hemoglobin in red blood cells to dilate small blood vessels responsible for supplying oxygen to

organs, including the brain. Oxygen can be delivered effectively only with the aid of SNO. Dr. Stamler said, “It’s not about how much oxygen you carry in your blood; it’s about how much oxygen is delivered through blood flow.”

Because SNO facilitates delivery of oxygenated blood to organs, like the brain, it is thought that loss of SNO may contribute to age-related dementia. The Stamler lab discovered that SNO levels can be increased not only through therapeutics but also through exercise and that not all forms of exercise are the same for this purpose.

Dr. Stamler and colleagues are developing a biosensor-based wearable device for use while exercising to measure levels of SNO and maximize exercise efficiency. Soon, people may use smart watches and fitness wearables to track their personal SNO levels, seeing real-time increases in their baseline SNO and brain fitness levels with exercise.



**1/3**

OF ISCHAEMIC HEART DISEASE CASES GLOBALLY IS ATTRIBUTABLE TO HIGH CHOLESTEROL



**262M**

PEOPLE WORLDWIDE SUFFER FROM ASTHMA



**1 in 3**

SENIORS IN THE US DIES WITH ALZHEIMER’S OR ANOTHER DEMENTIA



FOR MORE INFORMATION:  
[HarringtonDiscovery.org/Investigators/Stamler](http://HarringtonDiscovery.org/Investigators/Stamler)



# HARRINGTON SCHOLAR PROGRAMS

Our four Innovation Centers focus on unmet medical need. We support physicians and scientists in their development of new medicines across a broad range of diseases through our funding programs.



## **MAJOR DISEASES**

### **HARRINGTON SCHOLAR-INNOVATOR AWARD**

Supports physician-scientists whose research has the potential to change the standard of care in medicine. Each year, 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.

### **HARRINGTON-MSTP SCHOLAR AWARD AT CASE WESTERN RESERVE UNIVERSITY**

**In partnership with Case Western Reserve University (CWRU)**

Supports Medical Scientist Training Program (MSTP) students whose research shows innovation and creativity, and the potential for progressing from scientific discovery to a medical therapy.



## **BRAIN HEALTH MEDICINES**

### **HARRINGTON BRAIN HEALTH MEDICINES SCHOLAR AWARD**

Supports researchers whose work aims to treat or prevent Alzheimer's disease and related dementias.

### **ADDF-HARRINGTON SCHOLAR AWARD**

**In partnership with the Alzheimer's Drug Discovery Foundation (ADDF)**

Supports research efforts that seek to prevent, treat, or cure Alzheimer's disease, related dementias and cognitive decline associated with aging.

### **GUND HARRINGTON SCHOLAR AWARD**

**In partnership with Foundation Fighting Blindness (FFB)**

Supports innovative researchers who seek to translate their findings in retinal degenerative diseases into new therapies to improve and/or restore vision.



## **RARE DISEASES**

### **HARRINGTON RARE DISEASE SCHOLAR AWARD**

**Sponsored by Takeda Pharmaceutical Company Limited**

Supports researchers whose discoveries show promise for translation into novel medicines for rare diseases.

### **HARRINGTON UK RARE DISEASE SCHOLAR AWARD**

**In conjunction with Harrington Discovery Institute's registered UK charity, Fund for Cures UK**

Supports UK researchers who are advancing promising research into novel treatments for rare diseases, with the opportunity for funding and personalized drug discovery and development support.



## **COVID-19**

### **HARRINGTON SCHOLAR AWARD FOR CORONAVIRUS**

Supports promising, near-term treatments for the novel Coronavirus and its co-morbidities, and accelerates next-generation vaccines to avert future pandemics, as part of a broader initiative to aid in the global fight against COVID-19.



FOR MORE INFORMATION:  
[HarringtonDiscovery.org/Funding](https://HarringtonDiscovery.org/Funding)

# CONGRATULATIONS NEW SCHOLARS



## 2023 HARRINGTON SCHOLAR-INNOVATORS

**KIRK CAMPBELL, MD**

Icahn School of Medicine at Mount Sinai

**BERGE MINASSIAN, MD**

UT Southwestern

**MING-RU WU, MD, PhD**

Dana-Farber Cancer Institute

**JACQUES GALIPEAU, MD**

University of Wisconsin – Madison

**MICHAEL PACOLD, MD, PhD**

New York University

**TIMOTHY YU, MD, PhD**

Boston Children’s Hospital

**WON JIN HO, MD**

Johns Hopkins University

**ANTHONY ROSENZWEIG, MD**

University of Michigan

**MAXIMILLIAN KONIG, MD**

Johns Hopkins University

**JEFFREY SCHELLING, MD**

Case Western Reserve University

---

## 2023 HARRINGTON-MSTP SCHOLAR

**JENNINGS LUU**

Case Western Reserve University

---

## 2022 HARRINGTON-MSTP SCHOLAR

**WILLIAM WULFTANGE**

Case Western Reserve University



## **BRAIN HEALTH MEDICINES**

### 2022 ADDF-HARRINGTON SCHOLARS

**DONALD WEAVER, MD,**

**PhD, FRCPC, FCAHS**

University Health Network

**PAUL TESAR, PhD**

Case Western Reserve University

---

## 2022 VINNEY SCHOLARS

**NABIL ALKAYED, MD, PhD**

Oregon Health and  
Science University

**XIN QI, PhD**

Case Western Reserve University



# MEET OUR 2021 AND 2022 HARRINGTON SCHOLARS

# MAJOR DISEASES

DEVELOPING TREATMENTS FOR MAJOR DISEASES, SUCH AS LUNG, HEART AND CANCER IN AREAS OF UNMET NEED

## HARRINGTON IMPACT

**1,242**

TOP TIER  
DISCOVERIES

**11**

MEDICINES IN  
THE CLINIC

**22**

COMPANIES  
LAUNCHED

**1,900+**

TECHNOLOGY  
PROPOSALS

**18**

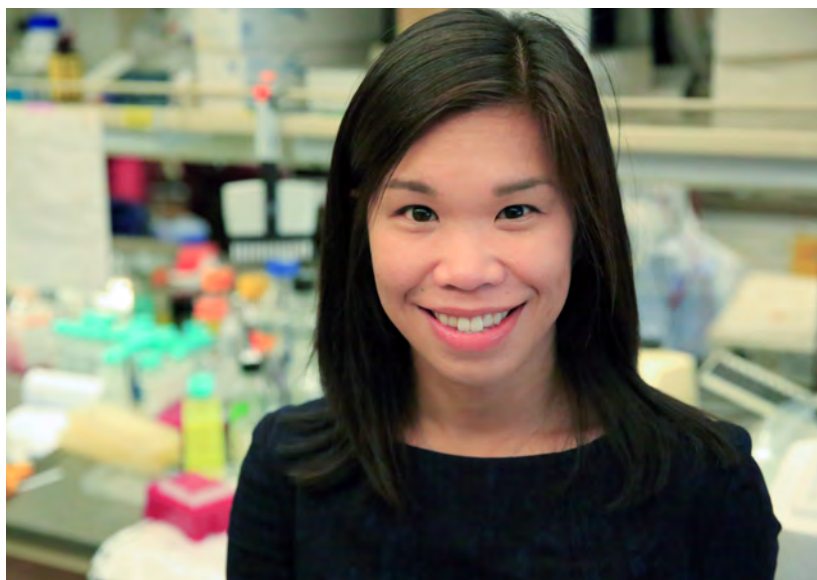
LICENSES  
TO PHARMA

**108**

MEDICINES IN  
THE MAKING

**JENNIFER CHEN, MD**

Assistant Professor, Department of Medicine  
University of California, San Francisco



## DEVELOPING NEW THERAPIES FOR FIBROTIC DISEASES

### FOCUS: Targeting acid ceramidase to reverse NASH fibrosis

Approximately 30 million Americans have nonalcoholic steatohepatitis (NASH), a chronic inflammation of the liver that can lead to serious damage in the form of scarring (cirrhosis) or liver cancer. There are no FDA-approved therapies for its treatment.

Dr. Jennifer Chen and her colleagues at UCSF have identified a novel antifibrotic target: acid ceramidase (aCDase). In preclinical studies, deletion or inhibition of aCDase leads to inactivation of hepatic stellate cells (HSCs), the primary cell type responsible for hepatic fibrosis. In mouse models, deleting aCDase in HSCs reduces fibrosis development and promotes fibrosis

regression. Treatment with an aCDase inhibitor also promotes fibrotic regression in cirrhotic human liver tissue *ex vivo*.

“While doing my clinical work I was struck by how many of my patients had end-stage liver disease—particularly NASH,” Dr. Chen says. “Many didn’t know they had it, and there were no treatment options for them. As a physician-scientist trained in hepatology, I am passionate about identifying new targets and potentially developing therapies for these patients.”

Working toward the goal of creating a first-in-class small molecule aCDase inhibitor, Dr. Chen and her colleagues are

performing lead series optimization and confirming the efficacy of developmental compounds using *in-vivo* and *ex-vivo* models of NASH. Ensuring that the compounds can be made orally available is a major focus.

Dr. Chen says she is impressed by how collaborative the process has been with the Harrington team.

“We’ve developed so many great partnerships,” she says. “I think that really highlights how important it is to understand fibrotic diseases and develop new therapies, because there is such a huge unmet need.”

*“Harrington Discovery Institute is completely dedicated to ensuring that our project moves forward. I feel so lucky to be in this community of people who are totally invested in our success.”*



SAVING LIVES BY

# TARGETING BAD CHOLESTEROL

**FOCUS:** Inhibiting PCSK9 self-proteolysis to treat atherosclerosis

Atherosclerosis—hardening and narrowing of artery walls caused by a buildup of cholesterol plaques—is a major risk factor for cardiovascular disease and stroke, the leading causes of death in the United States. A primary driver of atherosclerosis is elevated levels of low density lipoprotein (LDL), sometimes called ‘bad cholesterol,’ in the blood, and the protein PCSK9 is a contributor to elevated LDL levels. PCSK9 downregulates the hepatic LDL receptor, which clears LDL from the bloodstream. This downregulation raises LDL levels and accelerates atherosclerosis.

Dr. Chorba and his colleagues are pursuing a small molecule approach to inhibit the action of PCSK9 but are challenged by the fact that its biochemical output is difficult to study. Proteolysis (cleaving or breaking down of a protein) is required for PCSK9’s effect on the LDL receptor. However, as a single-turnover protease, PCSK9 cleaves only once; afterwards there is no further readout of its protease activity.

Dr. Chorba and his colleagues have developed a cell-based method to evaluate PCSK9’s proteolytic activity. They created a 70,000 compound high-throughput screen resulting in hit compounds that act as inhibitors of PCSK9’s proteolytic function. The researchers theorize that the development of a lead compound acting by its this novel mechanism of action will increase hepatic LDL receptor function and lower serum LDL.

“I think there are more mechanisms we can use to target PCSK9 than were previously thought,” Dr. Chorba says. “There are individuals who have mutations in PCSK9 where their PCSK9 simply doesn’t work. Our strategy, at least in theory, would mirror some of those mutations.”



**JOHN CHORBA, MD**

Assistant Professor, Department of Medicine  
University of California, San Francisco

*“As a junior investigator I really appreciate our Harrington advisors. They know the material, share ideas, and provide direction to keep the project moving forward.”*

**JOSEPH CONTESSA, MD, PhD**

Professor and Vice Chair of Therapeutic Radiology  
Yale University School of Medicine



## A NEW TARGET IN ONCOLOGY

**FOCUS:** Development of OST inhibitors for the treatment of lung cancer

A new concept for an oncology drug that has the potential to cure non-small cell lung cancer (NSCLC) is being pursued by Dr. Contessa and his colleagues.

Cell surface receptor tyrosine kinase (RTK) signaling is known to drive NSCLC initiation, proliferation, and tumor cell survival. Its correlation with the development and progression of numerous cancers has made RTKs an attractive therapeutic target. Dr. Contessa and his colleagues have studied RTK glycosylation as a new vulnerability for blocking RTK activity. Their work identified a first-in-class glycosylation inhibitor that targets the oligosaccharyltransferase (OST). This small molecule, called N-linked glycosylation inhibitor-1, causes OST to “skip” discrete cellular glycosylation sites. Using OST inhibitors in mouse models caused NSCLC tumors to regress.

“We looked at mechanisms of tumor cell resistance to other therapies, and they frequently rely on other receptors that require glycans for function,” Dr. Contessa says. “So we just asked the question, ‘Can we block addition of the glycans?’ At first the answer was no, because there was no small molecule that had that ability. So we performed high-throughput screening of chemical libraries to identify compounds that do have that effect.”

Dr. Contessa’s team, along with New England Discovery Partners, has synthesized hundreds of new analogs of N-linked glycosylation inhibitor analogs to enhance the potency and solubility of this drug class. With the assistance of Harrington Discovery Institute, they hope to expedite the move into clinical trials.

“This pathway has never been investigated in oncology before,” Dr. Contessa says. “We’re in a completely new space.”

*“Harrington has provided us with advisors that now comprise the only think tank in the world focused on understanding OST inhibitors.”*

## A QUEST FOR THE FOUNTAIN OF HEALTH



**TOREEN FINKEL, MD, PhD**  
Director, Aging Institute  
University of Pittsburgh

---

### **FOCUS:** A small molecule NAMPT activator to reverse age-dependent decline in NAD+

---

Good health is the wish traditionally conveyed by toasts in cultures around the world. Dr. Finkel, however, is doing more than simply raising a glass and wishing; he is conducting research into aging with the goal of helping humans remain healthier longer.

Nicotinamide adenine dinucleotide (NAD+) is a critical coenzyme found in every cell of the human body, and is involved in hundreds of metabolic processes. Aging is associated with a decline in tissue NAD+ levels, and this decline has been linked to various age-related diseases.

Dr. Finkel and his colleagues are researching the effects of restoring

NAD+ levels with a small molecule that augments the activity of NAMPT, the enzyme that controls NAD+ levels. Boosting or restoring NAD+ levels could represent a potential preventive therapy for a wide range of age-related diseases.

Dr. Finkel and his team developed an innovative screening platform to identify—from an initial library of more than 100,000 compounds—a set of small molecules that directly bind to NAMPT. They further determined that a subset of these binding molecules can potentially augment NAMPT activity. This approach thereby represents a novel overall strategy to modulate NAD+ levels.

Dr. Finkel is quick to point out that this research is not a quest for the mythical Fountain of Youth.

“We’re not really trying to extend lifespan,” Dr. Finkel says. “We’re trying to expand ‘healthspan,’ which is basically the time that individuals live free of diseases. The goal is to identify targets that link aging and disease and reduce the diseases and morbidities individuals face in their last few decades.”

*“Working with Harrington is about more than the funding: it’s about the people.”*

**AARON SCHIMMER, MD**

Professor, University of Toronto  
 Director of Research, Senior Scientist, Staff Physician  
 Princess Margaret Cancer Centre



## TARGETING

# VULNERABILITIES IN LEUKEMIA CELLS

**FOCUS:** Development of novel inhibitors of human mitochondrial protease ClpP

Acute myeloid leukemia (AML), a cancer that starts in the blood-forming cells of the bone marrow, is a disease with generally poor outcomes. The prognosis is especially poor in older patients and those with high-risk cytogenetics, who have a two-year survival rate of less than 15%.

Standard treatment for AML is intensive chemotherapy, possibly augmented by allogeneic stem cell transplantation. The combination, however, is frequently not curative and often provides only brief remissions. Therefore, Dr. Schimmer and his colleagues have developed strategies to target vulnerabilities in

leukemia cells in the mitochondria, downstream of the genetic mutations.

“Targeting the unique mitochondrial biology in AML may provide new therapeutic options,” Dr. Schimmer says. “Certain AML cells and their progenitor stem cells have the unique metabolic vulnerability of an increased reliance on the mitochondrial protease ClpP. Inhibiting ClpP chemically or genetically kills AML cells that have high ClpP expression, but doesn’t kill normal cells.”

A high-throughput shRNA screen of 140,000 compounds identified two novel chemical series that inhibited ClpP enzymatic activity

and killed ClpP- dependent AML cells. With the assistance of Harrington Discovery Institute, Dr. Schimmer and his team are working to develop and test small molecule agents that selectively inhibit ClpP. These ClpP inhibitors have the potential to target leukemic cells with high-risk mutations and also effectively eradicate the stem cell population that is a primary cause of disease relapse.

Dr. Schimmer notes that, if successful, these agents could potentially be useful not only in leukemia, but other malignancies as well.

*“In drug discovery, it’s always helpful to have seasoned veterans like our Harrington advisors at the table.”*



## A NOVEL APPROACH

## TO SHUT DOWN PANCREATIC CANCER

**FOCUS:** Targeted nanoparticle for early diagnosis and treatment of pancreatic cancer

Pancreatic cancer is a fatal disease resulting in about 50,000 deaths annually in the United States. From the time of diagnosis, the median survival ranges from 3 to 6 months. A “theranostic” approach combining early detection with target-specific nanoparticle (NP) gene therapy could transform heartbreak into hope.

Pancreatic precancerous lesions, or PanINs, have remained invisible on routine computerized tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasound imaging (EU). So far, PanINs evade detection until cancer develops and begins to metastasize. Growth of these lesions leads to 85% of pancreatic cancers diagnosed in the US. Using a nanoparticle and gene therapy platform, Dr. Jill Smith and her team seek to locate and shut off proteins driving the growth of pancreatic cancer.

“We discovered a receptor protein, CCK-BR, expressed in high-grade, precancerous PanIN lesions that is found in pancreatic cancer,” explains Dr. Smith. “We designed a NP (a particle one-billionth of a meter in size) with a peptide on the end that specifically targets and binds to CCK-BR. We labeled the NP with a fluorescent substance to image its path after injection. Staining showed it goes straight to the receptor and concentrates in PanIN lesions. In mouse models, we found no accumulation or toxicity in other organs.”

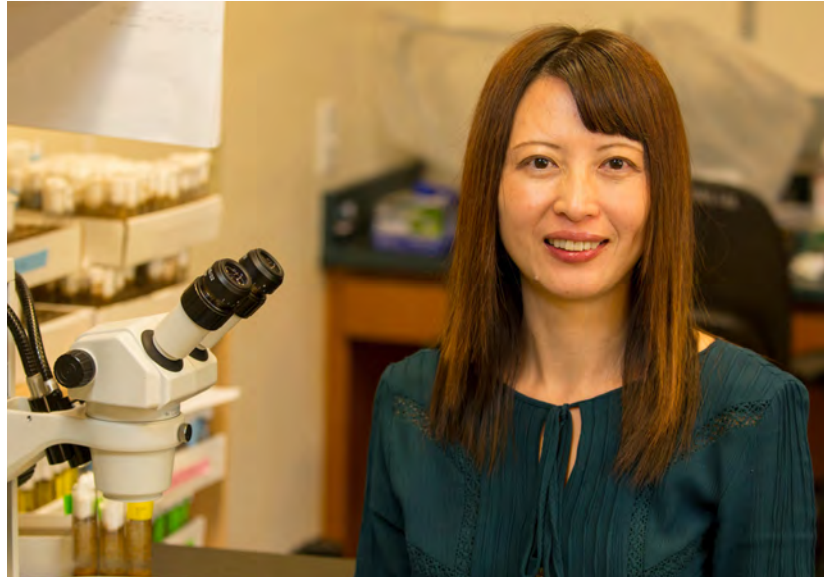
The approach also has potential with chemotherapy by aiding in detection and penetrating dense fibrosis, as well as treating other cancers where the CCK-B receptor is overexpressed,” she says. “Thanks to support from Harrington, our paper has been published in the prestigious International Journal of Molecular Sciences, and we can share our findings.”



**JILL SMITH, MD**  
Professor of Medicine  
Georgetown University

*“Our Harrington advisors are insightful and brilliant scientists.”*

**XINNAN WANG, MD, PhD**  
Associate Professor of Neurosurgery  
Stanford University



## A NOVEL STRATEGY FOR RESTORING **BRAIN CELL FUNCTIONING**

### **FOCUS:** Targeting mitophagy for treating Parkinson's disease

A pioneer in the study of mitochondria, which are the body's cellular power plants, Dr. Xinnan Wang discovered how misregulation of a transport protein called Miro1 leads to buildup of mitochondrial waste that results in degeneration of brain cells (neurons). Dr. Wang's team was the first to link this breakdown to Parkinson's disease (PD), a leading cause of cognitive and physical disability afflicting 1% of Americans over age 60, and 4% over 80 years. Miro1 is a hopeful target for developing a new class of drugs to battle PD.

"As humans live longer lives, more people will suffer from the effects of neural

degeneration," Dr. Wang explains. "Our strategy to couple Miro1-based therapy with a Miro1-dependent companion diagnostic tool could benefit millions of people worldwide."

Miro1 plays a role in keeping cells healthy through mitophagy, an intracellular mechanism that removes old, damaged mitochondria and cellular waste products. If this "housekeeping" process is malfunctioning, cells become weakened. Tragically, patients are not diagnosed with PD until close to 50% of their brain cells are affected. Current drug therapy only

treats the symptoms, including muscular tremors, speech, and mobility issues.

"With Harrington's help, our goal is to develop a blood test as well as an orally administered drug," Dr. Wang says. "Having identified the Miro1 biomarker, we envision potential to treat people with PD not only when they already have the disease, but also to delay the disease with early treatment before symptoms begin in at-risk individuals."

*"As a biologist barely experienced with drug chemistry, the help I've gained from my Harrington team is tremendously valuable."*

## HELPING PATIENTS BREATHE EASIER



### BURTON DICKEY, MD

Professor, Department of Pulmonary Medicine  
The University of Texas MD Anderson Cancer Center

#### FOCUS: Targeting Syt2 to prevent airway mucin hypersecretion

Human lungs have a remarkable self-cleaning system. Polymeric mucins are secreted into the airway lumen to form mucus. The mucus is continuously propelled out of the lungs by the rhythmic sweeping of fine, hair-like cilia, taking with it inhaled particles and pathogens. This innate defense system typically protects the lungs very well, but dysfunction in it can contribute to serious diseases including asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis.

“As long as you have the normal low level of mucin being slowly and steadily secreted, everything works fine,” Dr. Dickey explains. “But when the airway

senses threats, one of its responses is to dramatically increase the production of mucin. A sudden, massive release of highly expressed mucin can overwhelm the airway’s hydration capacity, creating excessively viscoelastic and adhesive mucus that results in airflow obstruction and lung inflammation.”

Some researchers are trying to control the excessive production of mucin, but Dr. Dickey and his team are taking another path and seeking to prevent its sudden release.

Dr. Dickey and his colleagues, along with structural biologist Axel Brunger of

Stanford University, had previously identified the calcium sensor Synaptotagmin-2 (Syt-2) as the trigger for rapid mucin secretion. Now they have identified a stapled peptide that protects against airway obstruction by inhibiting Syt2 interaction with the airway epithelial cell secretory machinery. They propose developing this lead compound as an inhaled therapeutic for the treatment of muco-obstructive lung diseases.

With the help of their Harrington advisors, Dr. Dickey and his team are working to improve the molecule and give it optimal characteristics before going into clinical studies.

*“The Harrington team has a good understanding of these early stages of drug development. They know where we are and what we should do next.”*

STRIVING TO MAKE PARALYSIS

# A THING OF THE PAST

**FOCUS:** Engineered human PMSCs for the treatment of acquired spinal cord injury

Nearly 1.5 million Americans suffer from some form of spinal cord injury. Dr. Farmer and her colleagues have successfully used early-gestation chorionic villus-derived engineered placental mesenchymal stromal/stem cells (PMSCs) to “dramatically and consistently” cure spina bifida-associated paralysis in lamb models. They also recently launched the first-in-human clinical trial to test PMSCs for the treatment of spina bifida.

Given their success using engineered PMSCs in congenital models of spina bifida, Dr. Farmer and her team are looking to

further develop this technology for adult-acquired spinal cord injury. They note that the application of placental stem cells for spinal cord injuries remains largely unexplored.

“Can we leverage a great discovery from one disease to another?” Dr. Farmer asks. “When we saw the profound effect of this therapy in our lamb models of spina bifida, we felt that we owed it to the world to investigate whether we could help patients with other kinds of spinal cord injuries that resulted in paralysis. It seemed to us that we had a moral responsibility to do so.”

In their preclinical work, Dr. Farmer and her colleagues have found that PMSCs seeded on an extracellular matrix scaffold and directly applied to the spinal cord injury site protect neurons and preserve spinal cord material.

If successful, such a PMSC-based regenerative treatment could lay the foundation for future clinical therapeutics to dramatically improve the quality of life for spinal cord injury patients.

**DIANA FARMER, MD**  
Distinguished Professor of Surgery  
University of California, Davis



*“Harrington is committed to helping us find answers. They share our curiosity.”*



NEW HOPE FOR

# REVERSING LUNG FIBROSIS

**FOCUS:** Thy-1 molecular mimicry as a therapeutic strategy for pulmonary fibrosis

Progressive pulmonary fibrosis (PPF) is a debilitating, often-fatal scarring process complicating many acute and chronic lung diseases, including COVID-19. Existing FDA-approved drugs only slow the progression of PPF. No curative therapy exists.

Dr. Hagood, a pediatric pulmonologist, and Ronit Freeman, PhD, an associate professor of applied physical sciences at UNC, have developed molecular mimics for a cell surface matrix-interacting glycoprotein, Thy-1. The mimics function as fibrosis suppressors via modulation of profibrotic signaling molecules at the surface of activated fibroblasts. In vitro, the mimics have shown the ability to restore homeostatic functions of profibrotic human lung fibroblasts. In mouse models of PPF, the mimics have reversed established fibrosis and restored lung architecture.

“The discovery that we could actually reverse the fibrosis was very exciting,” Dr. Hagood says. “This clinician-researcher collaboration is a potential game-changer for those facing the grim reality of PPF and other forms of chronic fibrosis.”

With funding from Harrington Discovery Institute, Drs. Hagood, Freeman, and their colleagues are now testing the effectiveness of their developmental peptide drug, mPep, in precision-cut lung slices generated from donor human lungs with the goal of developing a first-in-class therapeutic agent to reverse PPF.

Dr. Hagood adds that if successful, the mPep strategy may also be relevant in the future for additional indications including fibrosis of the liver, kidneys, and heart.



**JAMES HAGOOD, MD**

Professor of Pediatrics (Pulmonology)  
University of North Carolina at Chapel Hill

*“It will be transformational for us to have Harrington’s decades of drug development expertise going forward.”*

**LI LAN, MD, PhD**  
Associate Professor  
Massachusetts General Hospital Cancer Center



## CONVERTING RESISTANCE INTO RESPONSE

### FOCUS: Targeting mRNA methyltransferase in cancer therapy

Elevated oxidative stress and DNA replication stress are a double-edged sword in cancer cells. These intrinsic stresses promote tumor initiation and progression, but they also render cancer cells sensitive to radiation and chemotherapies. Dr. Lan and her colleagues are studying how cancer cells—specifically in breast and ovarian cancer—respond to oxidative and replication stresses through DNA repair pathways, and are developing new strategies to target these pathways.

Patients with breast and ovarian cancer are typically treated with chemotherapy drugs, including those that are platinum-based. Other cancer patients have benefitted from

targeted therapy such as PARP inhibitors (PARPi). PARPi improves survival in homologous recombination (HR) deficient patients with mutations of certain HR genes. Unfortunately, only around 10 to 20% of patients benefit from targeted therapy and almost all of the patients develop drug resistance.

Dr. Lan's team recently discovered and delineated a novel DNA repair pathway—mRNA-mediated repair. They found that inhibition or loss of the RNA methyltransferase TRDMT1 kills cancer cells with selective markers, and sensitizes HR proficient cancer cells

to PARPi and platinum. Therefore, it could convert PARPi- and platinum-resistant patients into PARPi and platinum super responders.

“When we first identified this RNA-dependent DNA repair pathway in 2015 the concept was too new to be accepted in the field,” Dr. Lan says. “Today many other groups have begun to see the importance of RNA in the DNA response.”

Dr. Lan's team has developed several lead compound TRDMT1 inhibitors; next steps include completing an IND application and testing the compounds' ability to suppress tumor growth in vivo.

*“It's very encouraging to have Harrington's resources and support at the critical stages of compound development and evaluation.”*

## SENDING SKIN CANCER INTO RETREAT

**FOCUS:** A repurposed small molecule to treat cutaneous squamous cell carcinoma

Cutaneous squamous cell carcinoma (cSCC) affects approximately 660,000 individuals in the US annually. Caused by exposure to ultraviolet radiation from sunlight or tanning beds, abnormal skin cells grow at an uncontrollable rate. Identification of a cSCC oncogene target, RET (REarranged during Transfection) and understanding of its downregulation, places early intervention within reach.

“While improved treatment options for metastasized skin cancer are needed, catching cancer in the early stages is even more critical,” says Dr. Carolyn Lee, a physician-scientist and dermatologist who conducts keratinocyte carcinoma screening and treatment at the Veterans Affairs Palo Alto Health Care System.

RET signaling is essential to normal development and maturation of many tissues, but deregulation of its activity contributes to tumor growth in multiple cancers including cSCC. One approach to preventing cSCC is treating precursor lesions, or actinic keratoses

(AK), which affect 50 million Americans yearly. Dr. Lee and her team are working toward an effective topical RET inhibitor, which they envision will provide therapeutic cSCC prevention in at-risk persons, such as those with AK.

“Our data indicate RET is activated early in the progression of normal skin to cSCC, and we plan to reverse this action with a topical RET inhibitor that stimulates immature cancer cells to evolve into mature non-dividing forms,” she explains.

The approach has been successful with other cancers, including acute promyelocytic leukemia.

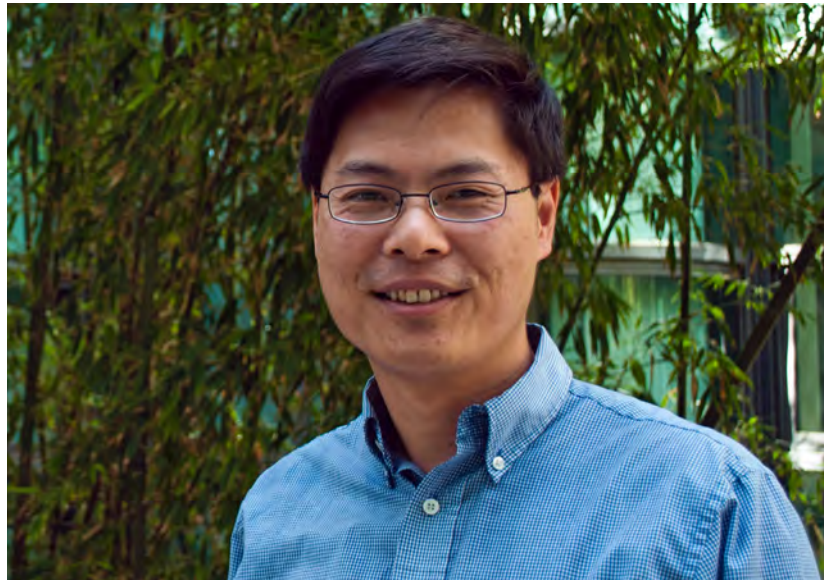
“With Harrington’s support, we aim to reduce the incidence of skin cancer with a topical medication option that will be well-tolerated by many, but particularly our military veterans who have sacrificed so much,” Dr. Lee added.



**CAROLYN LEE, MD, PhD**  
Assistant Professor of Dermatology  
Stanford University

*“Our Harrington advisors suggested we use computational modeling to prioritize designs for RET inhibition.”*

**MICHAEL LIN, MD, PhD**  
Associate Professor of  
Neurobiology, of Bioengineering  
and, by courtesy, of Chemical  
and Systems Biology  
Stanford University



## BETTER ANTIVIRALS FOR THE LONG TERM

**FOCUS:** Engineering an antiviral to combat COVID and its variants

Since March 2020, Dr. Michael Lin and his team have been testing candidate compounds for a drug that could be taken orally soon after a positive COVID-19 test – and also would be effective against emerging SARS-CoV-2 variants. Early treatment would save millions of immunocompromised individuals from hospitalization and potential complications stemming from the virus.

Central to Dr. Lin's focus are proteases (virus-encoded enzymes involved in viral replication). Having worked with protease inhibitors for the treatment of hepatitis C virus (HCV), Dr. Lin recognized similarities between HCV and SARS-CoV-2 viruses

leading him to target the SARS-CoV-2 main protease (Mpro).

"The coronavirus main protease is an attractive drug target because it's essentially the first catalytic event required for viral replication," Dr. Lin explains. "If you can make a drug that binds to the main protease and inhibits activity, then you can shut down viral replication from the very earliest time point."

The Lin Lab is tackling the challenges of developing an orally administered compound from two directions. While working to further improve

pharmacokinetics of the protease inhibitors they initially engineered (supported by the Wallace H. Coulter Foundation), they are investigating two promising tripeptide compounds with assistance from the Harrington Discovery Institute.

"What makes our project distinct from others is that we're not necessarily trying to find a good enough drug that can be done very quickly," Dr. Lin says. "We are trying to make this the best possible drug for the long term."

*"One of the main reasons we applied for the Harrington scholar program was for guidance with the initial new drug development process."*



A THERAPY FOR A COMMON PROBLEM

# EMERGES FROM A RARE DISEASE



## FRANCIS MCCORMACK, MD

Gordon and Helen Hughes Taylor Professor and Director  
Division of Pulmonary, Critical Care and Sleep Medicine  
University of Cincinnati

### FOCUS: An improved method of pleurodesis

Pneumothorax (collapsed lung) occurs when air leaks into the pleural space between the lung and chest wall, causing painful, labored breathing. Treatments range from observation to chest drainage. In cases where recurrence is likely, such as in the rare lung disease, lymphangioleiomyomatosis (LAM), talc pleurodesis is often used to irritate and fuse the pleural surfaces to prevent reaccumulation of air. Though effective, the talc never clears and is associated with lead exposure, chronic pain, and lung transplant complications. An improved method of pleurodesis is needed.

Rare lung disease expert and LAM therapy pioneer, Dr. Francis McCormack developed sirolimus as an FDA-approved therapy that stabilizes lung function decline in most LAM patients. The drug offers relief, but pneumothoraces still occur.

Dr. McCormack observed that calcium phosphate (hydroxyapatite) stones accumulate in lung alveoli of patients with pulmonary alveolar microlithiasis (PAM), another rare condition. Further noting that the body naturally decomposes the particles gave him the idea of using synthetic hydroxyapatite microspheres as a biodegradable approach to pleurodesis in

LAM cases. As effective as talc in mouse models, synthetic hydroxyapatite particles induce durable pleural fusion but are cleared from the pleural space within two months.

“I am grateful for many fruitful discussions with Harrington advisors from preclinical study design to partnering with industry for funding and licensing, and preparing for FDA approval of the hydroxyapatite particles method,” Dr. McCormack says. “Ultimately, this therapy may offer a safer pleurodesis approach for many common diseases associated with recurrent pneumothorax and recurrent pleural effusions.”

*“I look forward to the calls with the Harrington team. I feel heard, the discussions are lively and fun, and the advice and ideas are always illuminating.”*

## NEARLY NATURE: A NEW TREATMENT FOR CORNEAL BLINDNESS

**FOCUS:** In situ-forming regenerative extracellular matrix therapy for the cornea

Corneal blindness affects over 12.5 million people worldwide with less than 2% having access to a sight-restoring corneal transplant. A groundbreaking technique using a superglue-like gel is a hopeful cure.

Dr. David Myung and his lab have developed, and successfully tested in animal models, a novel biomaterial for filling and healing corneal defects.

The crosslinked compound, a proprietary blend of crosslinkable collagen and other materials, has the consistency of honey. Applied following surgical removal of scar tissue or used to backfill deep corneal wounds, the gel serves as a regenerative

extracellular matrix to support native corneal cells—the epithelium—to grow over the wound, and eventually be replaced entirely by transparent stromal tissue.

“Think of it as ‘biological spackle,’” Dr. Myung says. “A very small amount—less than a typical droplet of water—can fill even large defects, forming a solid gel that leaves the cornea the way it’s meant to be: smooth and clear.”

“Input from our Harrington advisors is crucial to making sound decisions about manufacturing, sourcing of materials, and FDA-requirements for characterization and testing,” Dr. Myung explains.

“Corneal transplants have been done the same way for a hundred years, by suturing donor corneas into place,” Dr. Myung says. “As effective as the procedure is, there’s always a risk of infection and rejection. Meanwhile, there is still a major shortage of graft tissue. We are hoping that our solution, which requires no sutures or graft tissue, can help address these limitations.”

### DAVID MYUNG, MD

Associate Professor of Ophthalmology at the Byers Eye Institute at Stanford and, by courtesy, of Chemical Engineering Stanford University



*“Our Harrington advisors are helping us to navigate a pathway to clinical trials and regulatory approval.”*

**BERND SCHNABL, MD**

Professor of Medicine in Gastroenterology  
University of California, San Diego

## FIGHTING ALCOHOLIC LIVER DISEASE

**FOCUS:** Deploying a bacteriophage army to eliminate cytolysin-producing bacteria

Bacteriophages, or phages, are naturally occurring viruses that destroy bacteria. These bacteria eaters are being harnessed as drugs for targeted treatment of alcoholic hepatitis (AH). With antibiotic resistance at alarming levels, phage therapy (PT) offers a potential alternative.

Cytolysin is a toxin generated by *Enterococcus faecalis* bacteria found in fecal samples from close to one-third of patients hospitalized with late-stage alcoholic hepatitis,” says Dr. Bernd Schnabl, a gastroenterologist by medical specialty. “All the blood from the intestine goes to the liver, which filters for

nutrients, toxins, and microbiota—microbial products. The liver begins to fail when it is overwhelmed with toxins like cytolysin. We have even seen some patients at the end stage of liver disease go into a coma and wake up when given antibiotics, confirming the causal relationship of improving health by destroying dangerous bacteria.”

With Harrington support, Dr. Schnabl and his team are conducting efficacy tests of synthetic, patentable phages for development of a universal drug for AH. But bacteriophages are very picky eaters, and matching the right phage to the right “food” is tricky.

“Some phages recognize toxin producing bacteria from multiple patients, some from one patient,” Dr. Schnabl says. “We have been editing and testing an ‘army’ of natural phages, which is expensive and time-consuming. So far, our first generation of phages can overcome bacterial resistance and destroy a broader range of bacteria than the parent phages. If cytolysin is linked to other diseases, the PT approach has potential for more novel antibacterial drugs.”

*“Our Harrington team is helping us move closer to a Phase 1 clinical study.”*

A NEW DRUG PLATFORM

# URNS CANCER AGAINST ITSELF

**FOCUS:** Multimodal targeting of chemoresistant cancer by stapled peptide PROTACs

A new weapon to fight acute myeloid leukemia (AML), and other relapsed and refractory cancers in children and adults, turns the enemy—cancer—against itself. The therapeutic approach uses a 3-in-1 modality, deploying a stapled (reinforced) p53 peptide proteolysis-targeting chimera (SP-PROTAC).

As guardian of the genome, p53 protects our cells from becoming cancerous. However, cancer can deploy its HDM2 and HDMX proteins to suppress p53 and activate oncogenic transcription by hijacking BET proteins. The Walensky lab designed a stapled p53 peptide

linked to a small molecule BET inhibitor to synergistically degrade BET proteins and maximally reactivate p53 pathway by targeting HDM2 and HDMX. Blocking multiple oncogenic signaling pathways at once causes cancer to self-destruct.

“We hijack HDM2—the cancer cell’s degrader of p53—and divert its attention to destroy cancer-causing proteins instead,” Dr. Walensky explains. “We simultaneously liberate p53 to resume its powerful tumor suppressor function.”

A chemical biologist and pediatric oncologist who cares for children with leukemia, Dr.

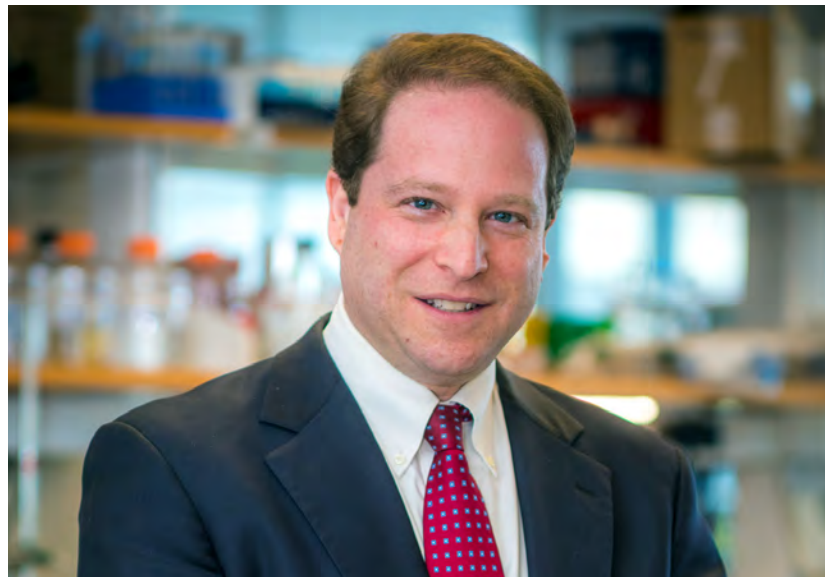
Walensky knows the challenges associated with cancer relapse and its treatment.

“We are laser-focused on achieving the benefits of multiagent therapy while minimizing the side-effects,” Dr. Walensky says. “We pack the biggest punch by targeting multiple cancer-causing pathways in the same cell at the same time, while also streamlining the clinical development path by advancing a single agent that does the job of three. Our Harrington advisors are an enormous asset—their insights and advice have been instrumental in helping us realize the full potential of our new drug modality.”

## LOREN WALENSKY, MD, PhD

Professor, Pediatrics, Harvard Medical School  
Professor, Pediatric Oncology, Chemical Biology  
Dana-Farber Cancer Institute

*“Without question, the monthly advisory meetings have sharpened our focus and expedited the pace of our progress.”*





HOPE FOR

# CHILDREN WITH NEUROBLASTOMA

**FOCUS:** Blocking MYC protein production in cancer

More than ten years ago, a research team led by Dr. Hans-Guido Wendel learned of the intriguing anti-cancer and antiviral properties of Silvestrol, a compound produced by the tropical *Aglaia foveolata* tree. The compound protects the tree against various pests. Dr. Wendel's lab demonstrated that it halts cancer growth—and showed how—leading to insights for novel drug development.

Silvestrol acts as a specific inhibitor of the RNA helicase, Eukaryotic Translation Initiation Factor eIF4A, an enzyme implicated in aberrant translation of protein mRNA. Increased activity of the enzyme contributes to aggressive cancers, such as pediatric neuroblastoma (NB), leukemias and brain cancers, and small cell lung cancer in adults.

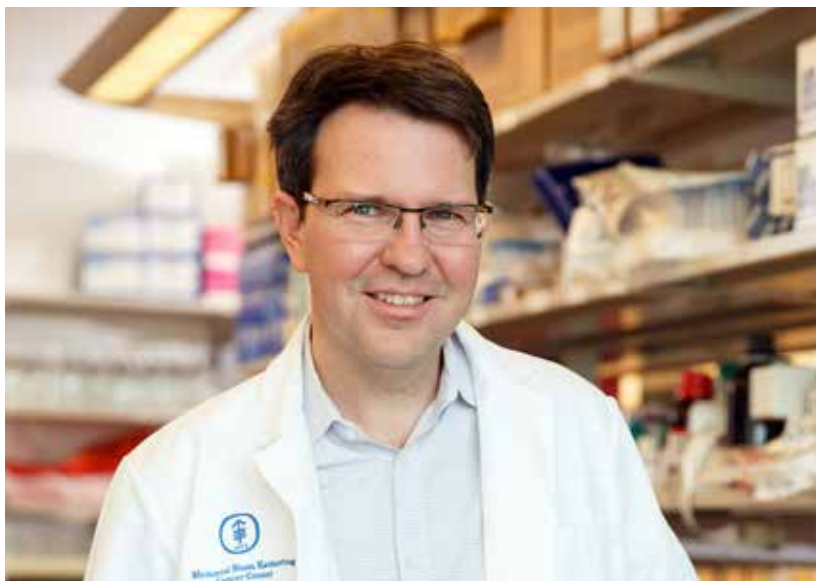
Specifically, the production of a common and well-known cancer growth driver, a protein called MYC (pronounced “mick”), depends on eIF4A. The Wendel lab team hypothesized that targeting MYC

by blocking its production would stop cancer growth quickly, so they began testing Silvestrol analogs.

“It was surprising to find such strong activity against cancer cells targeting mRNA translation,” Dr. Wendel says. “Previously, little thought had been given to stopping cancers by blocking production of the MYC protein.”

With the support of Harrington Discovery Institute, Dr. Wendel and his team are working to optimize the medicinal chemistry of Silvestrol analogs.

“Results of our initial eIF4A inhibition studies in cell culture and mouse models have been very exciting,” he says. “Our Harrington team has developed a highly creative IND-plan for making patentable compounds that have high affinity for the target. This is a great mechanism against many MYC-driven cancers such as lymphoma, neuroblastoma, and others.”



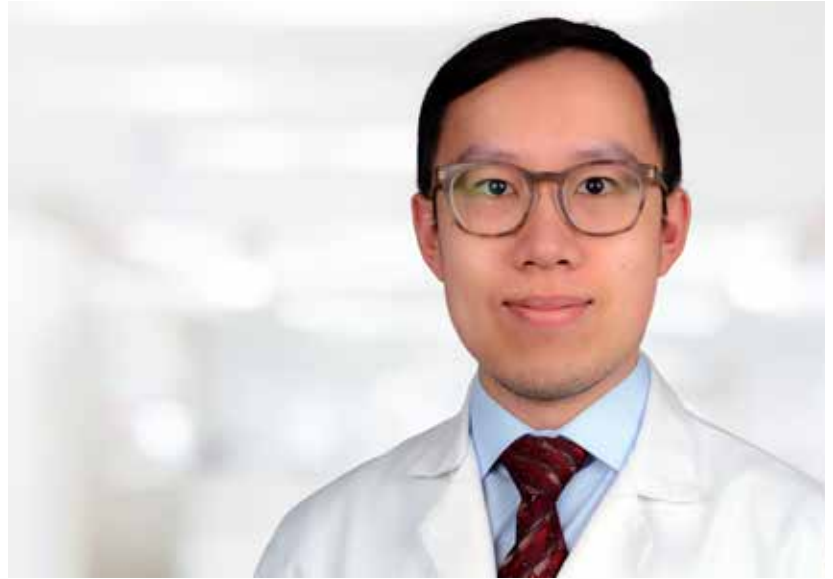
**HANS-GUIDO WENDEL, MD**

Professor, Cancer Biology & Genetics Program  
Memorial Sloan Kettering Cancer Center

*“Thanks to Harrington’s brilliant experts in medicinal chemistry, we are making major strides with analog development and testing.”*

**DEREK WONG**

Doctoral Candidate, Medical Scientist Training Program  
Case Western Reserve University



## OPTIMIZING A WEAPON TO FIGHT CANCER

**FOCUS:** Genetically modified, amped-up natural killer cells

B-cell malignancies encompass many different types of cancer, such as acute lymphoblastic leukemia (ALL), non-Hodgkin lymphomas (NHL), chronic lymphocytic leukemia (CLL) and multiple myeloma (MM). Chimeric antigen receptor (CAR) T-cell therapy has proven effective for the treatment of relapsed/refractory B-cell malignancies, but the high cost, complex manufacture, and adverse effects associated with CAR-T therapy leaves room for underexplored cellular immunotherapies, such as CAR-NK cells.

“Unlike CAR-T cells, the CAR-NK concept allows you to take natural killer (NK)

immune cells from a healthy donor and genetically modify, expand and freeze them, and then quickly deliver them to cancer patients when they need them. In essence, this is an ‘off the shelf’ treatment,” says Mr. Derek Wong.

B-cell activating factor (BAFF) is a protein that normally helps regulate B-cell development and survival, but BAFF receptors are also expressed by numerous B-cell cancers. Mr. Wong’s innovation combines the BAFF-CAR construct the lab already validated in T cells with NK cells to create BAFF CAR-NK cells.

“If the cancer cell expresses any of the B-cell activating factor receptors, our BAFF construct CAR-NK cells will target them,” Mr. Wong says.

With Harrington support, Mr. Wong and his team have further modified their BAFF-CAR construct to make them more specific for NK cells. They have narrowed down their designs to two novel, promising provisional patent candidates that have been effective against cancer cell lines in culture. “We hope our approach can be used to treat relapsed B-cell cancers, reinducing remission and prolonging patient survival,” Mr. Wong says.

*“The Harrington team is always encouraging and very interested in the data.”*

# BRAIN HEALTH MEDICINES

DEVELOPING TREATMENTS FOR NEURODEGENERATIVE DISORDERS,  
MENTAL HEALTH AND NEUROMUSCULAR DISORDERS

## HARRINGTON IMPACT

**188**

TOP TIER  
DISCOVERIES

**3**

MEDICINES IN  
THE CLINIC

**4**

COMPANIES  
LAUNCHED

**535+**

TECHNOLOGY  
PROPOSALS

**3**

LICENSES  
TO PHARMA

**25**

MEDICINES IN  
THE MAKING



## DEVELOPING A NOVEL TREATMENT FOR ALZHEIMER'S DISEASE

**FOCUS:** Leveraging exercise to improve cognitive function in Alzheimer's disease

Cognitive function is a serious medical and social challenge affecting an increasingly aging population. Alzheimer's disease (AD) alone affects an estimated 5.5 million Americans, and current drug treatment options are limited. But a new discovery linked to daily exercise holds promise for novel AD treatment.

"Regular physical exercise improves cognitive functions by stimulating adult hippocampal neurogenesis and reducing neuroinflammation," says Dr. Christiane Wrann. "We traced these effects to irisin, a natural hormone secreted from muscles in response to exercise."

The irisin hormone, which is the secreted form of FNDC5 (fibronectin-domain III containing 5), offers neuroprotection in aging brain cells, delaying neural degeneration while guarding against obesity, insulin resistance, and nonalcoholic fatty liver disease.

FNDC5, which is expressed in skeletal muscle and the brain, is upregulated in aerobic exercise. Dr. Wrann's preclinical research

in mice showed that genetic deletion of irisin impairs cognitive function while an increase improves memory and reduces brain inflammation.

With support from Harrington Discovery Institute and the Alzheimer's Drug Discovery Foundation (ADDF), the Wrann lab is investigating dosing strategies that allow enough irisin to cross the blood-brain barrier to do its work. They will also perform a proof-of-concept/principle study with recombinant irisin in preclinical Alzheimer mouse models.

"Surprisingly, our findings showed that irisin was not acting on neurons, but the astrocytes and microglia that nourish neurons so we can think, move, and breathe," Dr. Wrann said. "We can't rescue/revive neurons that have died/degenerated, but we believe irisin is a key to extending independent living—and that would be a huge win."

### **CHRISTIANE WRANN, DVM, PhD**

Associate Professor in Medicine  
Cardiovascular Research Center and the McCance  
Center for Brain Health at Massachusetts General  
Hospital and the Harvard Medical School



*"The industry perspective we have gained from our Harrington advisory team is tremendously valuable."*



## NEW HOPE FOR REVERSING VASCULAR DEMENTIA

**FOCUS:** Employing the GPR39 receptor to restore brain health

Vascular dementia affects about one-third of people over age 80, diminishing their thought processes and rendering them increasingly confused and helpless. With the assistance of Harrington Discovery Institute, researchers are validating a target receptor in the brain for a novel drug to detect, treat, and possibly, reverse this condition.

Dr. Nabil Alkayed is investigating the role of a vascular receptor in the brain called G protein-coupled receptor (GPR39). This receptor could be a key to preventing impaired function of microvessels, especially capillaries, tiny blood vessels less than one-tenth the diameter of a human hair that keep the brain healthy and functioning.

“The longer humans live, the more we will see vascular dementia. While the reason remains unknown, poor diet and unhealthy lifestyle choices accelerate and worsen the disease,” Dr. Alkayed explains. “What is actually vascular dementia is often called Alzheimer’s disease, a separate neurological condition. Frequently, cognitive impairment is caused by a combination of the two.”

Memory experiments in mice fed a high-fat diet will determine whether GPR39 improves recall by way of a mechanism that activates the receptor for protective factors called epoxyeicosatrienoates (EETs). Initial mouse memory testing yielded exciting discoveries: increasing

EETs by preventing their breakdown reversed memory loss and blocking EETs action by deleting GPR39 worsened memory loss.

“With neural degeneration, brain cells die and that’s it,” Dr. Alkayed notes. “In vascular dementia, the microvessels do not function properly. By restoring health to this vascular system, there’s hope for preventing and reversing dementia. Our work with Harrington will validate the role of GPR39 for doing that.”



**NABIL ALKAYED, MD, PhD**  
Professor of Anesthesiology and  
Perioperative Medicine  
Director of Research, Knight  
Cardiovascular Institute  
Oregon Health and Science University

*“We are grateful for our Harrington team’s guidance in study design and making the right choices for drug selection and method of delivery.”*

**XIN QI, PhD**  
 Professor, Department of  
 Physiology & Biophysics  
 Case Western Reserve University  
 School of Medicine



MOVING TOWARD

# MITOCHONDRIAL MEDICINE

**FOCUS:** Development of ATAD3A peptide inhibitor as a potential treatment for Alzheimer's disease

Mitochondria is a cellular organelle often referred to as “the powerhouse” because it generates energy fueling cell lifecycle processes. Evidence suggests that mitochondrial damage plays a critical role in the pathogenesis of Alzheimer's Disease (AD), Parkinson's (PD) and rare neurodegenerative diseases, such as Huntington's (HD) and amyotrophic lateral sclerosis (ALS). This makes it a viable target for both small molecule- and peptide-based treatment strategies to prevent or slow neurodegeneration that impairs memory and mobility.

“We know that mitochondrial dysfunction leads to neuropathology in HD and it occurs in early stage AD,” says Dr. Xin Qi, whose laboratory pioneers small molecule mitochondrial enhancers and the use of peptide inhibitors, such as DA1, HV-3, and P110, against mitochondrial dysfunction in various neurodegenerative diseases.

As a 2018 Harrington Rare Disease Scholar, Dr. Qi and team demonstrated efficacy of a small molecule compound,

CHIR99021, in patient brain cells and animals with HD to rescue mitochondrial proteostasis and bioenergetics. With support from the Harrington Brain Health Medicines Center, Dr. Qi is testing a peptide inhibitor aimed at the protein, ATAD3A, to prevent mitochondrial damage in AD.

“Our goal is to develop a target-specific ‘mitochondria medicine’ to delay onset of serious neurodegenerative symptoms and slow disease progression,” she explains.

Harrington support has proven invaluable in advancing Dr. Qi's academic science to drug development.

“One of our key Harrington advisors is a peptide chemist whose guidance has helped us improve medicinal chemistry for subcutaneous delivery,” she says. “We are working to achieve stability and increase half-life—prerequisites for animal safety studies and clinical trials. The project is running well and results are exciting!”

*“Far beyond lab experiments, Harrington has taught me there's much more work and collaboration involved in drug development.”*

# RARE DISEASES

DEVELOPING TREATMENTS FOR RARE AND  
ULTRA-RARE VARIANTS OF DISEASES

## HARRINGTON IMPACT

**235**

TOP TIER  
DISCOVERIES

**2**

MEDICINES IN  
THE CLINIC

**8**

COMPANIES  
LAUNCHED

**650+**

TECHNOLOGY  
PROPOSALS

**5**

LICENSES  
TO PHARMA

**36**

MEDICINES IN  
THE MAKING



# COVID-19

DEVELOPING TREATMENTS FOR CORONAVIRUSES  
AND PANDEMIC-CAUSING PATHOGENS

## HARRINGTON IMPACT

54

TOP TIER  
DISCOVERIES

4

MEDICINES IN  
THE CLINIC

1

COMPANY  
LAUNCHED

300

TECHNOLOGY  
PROPOSALS

3

LICENSES  
TO PHARMA

12

MEDICINES IN  
THE MAKING



# THE HARRINGTON ADVANTAGE



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

*“It’s not just an award, it’s a career-long relationship.”*

## RELATIONSHIPS ARE IN OUR DNA

Every scientist who submits a proposal for a Harrington Scholar Award is working on a potentially breakthrough new treatment or cure. Proposals are evaluated on a multitude of factors including novelty, clinical impact, the Principal Investigator (PI), competition, and the ability of the Harrington Therapeutics Development Center to help accelerate development of a medicine that would impact unmet need.

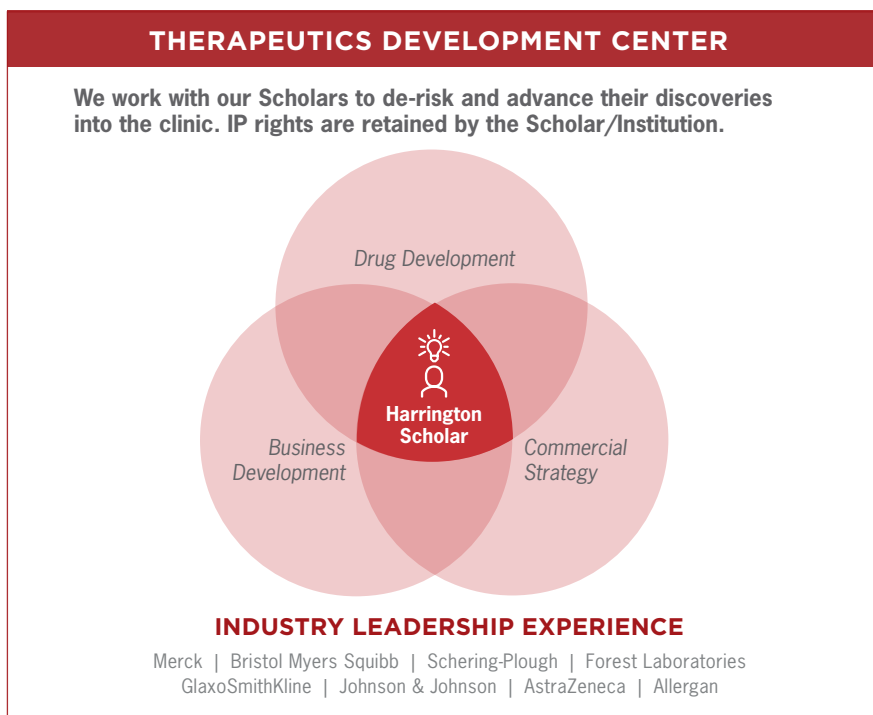
Most applicants have a good sense of what they will receive if selected for a Harrington award. They understand that the differentiating value is the access to world-class drug development expertise that is combined with funding.

What a PI may not realize is that the Harrington model supports a continuing relationship to help advance their project towards the clinic, and ultimately towards the approval of a new drug. Harrington’s Therapeutics Development Center (TDC) comprises 30-plus industry experts with a track record of bringing drugs to market, and a team of dedicated project managers who are able to run these academic lab projects as if they were a virtual Pharma. Our model works best when the PI incorporates our expert advisors and project managers as extended members of their lab team.

### Our TDC experts offer our scholars:

- Fundamental scientific knowledge—how will we develop this drug and how will it work;
- Regulatory pathway knowledge—what do we need to demonstrate for the FDA to test this new drug in humans;
- Commercial and market knowledge—how do we position the project so that the investor will get a good return on their investment.

At the core of our Harrington successes over the past 10+ years are the relationships we have built with our scholars. The specifics of the relationships may vary, but they are indeed career-long and have one thing in common: a shared goal of bringing new medicines to patients.



# A TWO-TIME HARRINGTON SCHOLAR'S PATH TO DEVELOPING A MITOCHONDRIAL MEDICINE

Xin Qi, PhD, an expert on mitochondria, is conducting preclinical testing of a peptide-based treatment for Alzheimer's disease (AD). She and her team are excited about the results and potential for treating other neurodegenerative diseases.

This is the second time Dr. Qi's work has been supported through Harrington Discovery Institute. As a 2018 Harrington Rare Disease Scholar, she developed a promising compound aimed at slowing progression of Huntington's disease (HD).

"Before my Harrington scholarship, I had limited drug development experience and knowledge, but that project opened my mind and eyes," she shares.

## SCIENTIFIC GROUNDING

A consummate scientist, Dr. Qi believes that maintaining a solid grounding in science is critical to success in the Harrington scholar programs. Her specialty is mitochondria, an organelle known as the cell's power plant. She and her team are focused on mitochondrial dynamics related to proteins in the regulation of mitochondrial function, genome stability, lipid metabolism, and

neuron-glia communication—and how the processes play out in neurodegeneration. Evidence also points to mitochondrial dysfunction in the pathogenesis of heart disease and cancer.

"Once you block something that occurs at a very early stage, you can prevent a disease from propagating even before the patient shows symptoms," Dr. Qi explains.

"Twelve years ago we started trying to understand how organelle damage is involved in neural degeneration in Huntington disease and Parkinson Disease," she relates. "We wanted to identify which molecule of mitochondria could be a drug target."

Currently, no cure or effective treatment is available for neurodegenerative disease, and Dr. Qi and her team are determined to develop a "mitochondria medicine" to effectively block neuron degeneration.

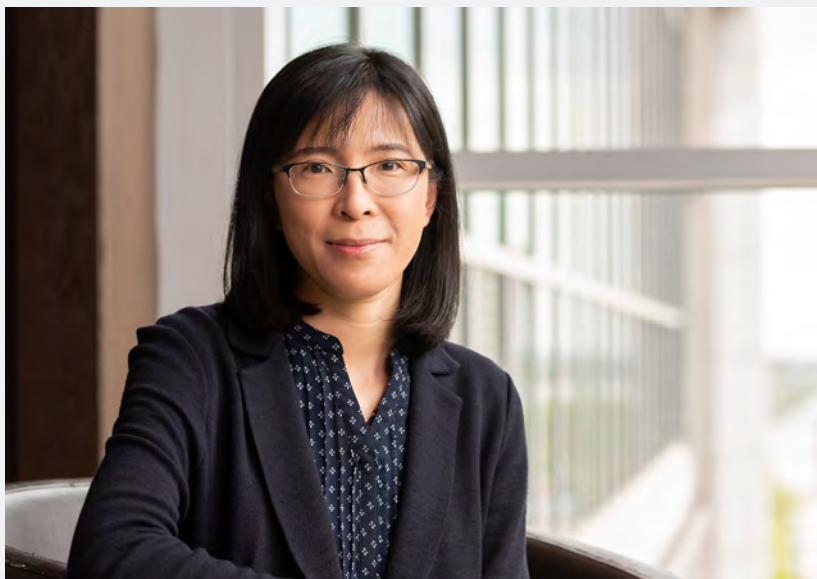
## A GUIDED JOURNEY

"The Harrington team of advisors provide a comprehensive view of the projects while providing support on all levels," Dr. Qi shares. "As a Harrington scholar, you are guided to

become very goal driven. You work closely with your Harrington project manager and learn how to set milestones for your project. The advisory team provides many recommendations, but you are responsible for carrying out the necessary work to ensure project success. If you do not follow their advice, you will not make progress."

Advisory team assistance is generous and readily available, and it contributes to tangible results. For example, running high throughput screening of more than 50,000 compounds with the help of her first Harrington advisor, Peter Bernstein, PhD, yielded a HD drug candidate, CHIR99021. As a potential HD treatment, the compound showed efficacy in animal models and human brain tissue testing—actually reversing motor deficits in the HD mice.

"Dr. Bernstein has provided invaluable guidance on medicinal chemistry and compound modification for both the HD and AD projects," Dr. Qi shares. "He is analytically minded and always responsive with thorough knowledge of drug development that has advanced the projects significantly."

**XIN QI, PhD**

Professor, Department of Physiology & Biophysics  
Case Western Reserve University School of Medicine  
2018 Harrington Rare Disease Scholar  
2022 Vinney Scholar, Harrington Brain Health  
Medicines Center

*“Harrington not only provides funding; they also support you. This is the best program!”*

Under the recent Vinney Scholar Award, Dr. Qi aims to refine a macrocyclic DA1 peptide targeting a specific mechanism (ATAD3A oligomerization) to reduce brain cholesterol accumulation while leveraging improved central nervous system drug properties.

Dr. Qi and her team have had to work at solving potential issues related to in vivo metabolic instability and short circulation time of the DA1 peptide. Modifications have improved stability and half-life, allowing her to proceed with efficacy testing in different animal models.

Peptide modification and study design assistance from William Murray, PhD, has been critical to the Vinney AD project, as has help from central nervous system (CNS) experts, Perry Molinoff, MD and Michael Ahlijanian, PhD. Dr. Qi’s project manager, Jeff Klein, PhD, MBA, PMP, has been instrumental in helping her leverage the breadth of Harrington resources, while ensuring the team meets project timeline and objectives.

“Dr. Murray directed our AD project and consistently made useful suggestions

that enabled us to be highly productive, while Dr. Molinoff’s and Dr. Ahlijanian’s insights on CNS aspects have informed certain lab processes,” Dr. Qi credits.

Collaborative spirit and a shared mission of bringing cures for today’s debilitating diseases are strong drivers for Dr. Qi and her team. There’s also Dr. Qi’s husband, who reminds her to hurry up and find a cure for Alzheimer’s disease: “He tells me, ‘I’m waiting!’”

**MULTIPLE AWARD HARRINGTON SCHOLARS****DAVID GAMM, MD, PhD**

University of Wisconsin – Madison

**BENJAMIN GASTON, MD**

Case Western Reserve University  
Indiana University

**JEFFREY GLENN, MD, PhD**

Stanford University

**XIANXIN HUA, MD, PhD**

University of Pennsylvania

**XIN QI, PhD**

Case Western Reserve University

**DONALD WEAVER, MD, PhD**

University Health Network

**TIMOTHY YU, MD, PhD**

Boston Children’s Hospital





## TAKING PRECISE AIM AT RHEUMATOID ARTHRITIS

As a youth, internationally recognized physician-scientist Dr. Nunzio Bottini heard his pediatrician-geneticist father say the word “phosphatase” a lot. The elder Dr. Bottini was referring to protein phosphatases, a group of catalyst enzymes.

“My dad was researching the role of enzymes in disease back in the 1960s,” recalls the 2016 Harrington Scholar-Innovator, who is a practicing rheumatologist and now the Inaugural Director of the Kao Autoimmunity Institute at Cedars-Sinai Medical Center in Los Angeles. “It sounds a bit corny, but I was imprinted early to be interested in protein phosphatases!”

“Now is an exciting time for phosphatase experts,” Dr. Bottini says. For a long time, protein phosphatases have been considered “undruggable,” but this view has changed recently and they are now emerging as key targets for several human diseases.”

### A CONNECTION IS MADE

Curious to learn why some people are predisposed to develop rheumatoid arthritis (RA) -the most common form of autoimmune arthritis- and what makes it more severe in some patients, the Bottini Laboratory at University of California, San Diego explored phosphatase genes in immune and non-immune cells. Their groundbreaking work led to a prize-winning report in 2015, in which they identified a specific phosphatase in specialized cells called fibroblast-like synoviocytes (FLS) that line the joints. The cells are nonimmune in nature but they promote inflammation leading to RA, invasively destroying the affected joint’s cartilage and contributing to bone erosion.

“Normally, phosphatases act as brakes, signaling the synoviocytes to ‘calm down,’ but when dysregulated, these proteins become silenced and cannot stop synoviocytes from acting up,” Dr. Bottini says. “The intervention we discovered and are trying to develop—the early work was with Harrington’s support during my

2016 project—restores the ‘voice’ of the phosphatase in the fibroblasts.”

### THE DRIVE TO RESOLVE UNMET MEDICAL NEED

“Advances in the last 20 years have changed the way we manage autoimmune arthritis and now we have medications that can alter the course of RA,” Dr. Bottini explains. “We’ve seen substantial improvement in therapeutics, but the standard treatments, commonly called disease-modifying antirheumatic drugs (DMARDs), and even the synthesized biologics approved in the 1990s (B-DMARDs), suppress the immune system. In certain patients, immune suppression can increase risk of infection and complicate treatment of other conditions. We need additional options.”

### DEVELOPING NEW PHOSPHATASE TARGETED BIOLOGICS

What if you could develop a drug that effectively controls autoimmune arthritis without the baggage of immunosuppressant



### **NUNZIO BOTTINI, MD, PhD**

Director, Kao Autoimmunity Institute,  
Cedars-Sinai Medical Center  
Co-Founder, Knoubis Bio, Inc.  
2016 Harrington Scholar-Innovator

*“My experience with the Therapeutics Development Center was not only enabling but had a transformative impact on me as an academic scientist.”*

effects? What if the drug could synergistically enhance or optimize existing RA medications by allowing physicians to use them at lower dose levels for patients who cannot tolerate immunosuppression? Dr. Bottini thinks all of this is possible. He looks to the promise of the phosphatase protein he is studying in synoviocytes as a druggable target and would like to develop a novel synthetic biologic that would locally control inflammation by inhibiting the damaging action of synoviocytes without affecting the body's immune defenses against infections or cancer.

### **THE PATH TO COMMERCIALIZATION**

Dr. Bottini is among the co-founders of Knoubis Bio, a company whose objective is to produce a first in class biologic that targets synoviocytes to achieve control of autoimmune arthritis without affecting the body's natural protective immune response. Dr. Bottini serves as a scientific advisor for the company. Dr. Paul Williamson—a pharmaceutical industry veteran who connected with Dr. Bottini through the Harrington Discovery Institute where he is a member of the Therapeutics Development Center - is also a co-founder of Knoubis Bio and serves as a key advisor for product development.

“The company is currently raising capital to optimize the lead product and initiate the appropriate preclinical and chemistry, manufacturing, and controls (CMC) work needed to gain FDA approval for clinical studies” says Dr. Bottini. Dr. Bottini is enthusiastic about helping Knoubis Bio develop a new approach for alleviating pain and suffering of arthritic patients who cannot tolerate immunosuppression. “We are excited that the continued support of Harrington Discovery Institute has enabled the innovation to reach this stage!”



### **HARRINGTON STAGE 2 AWARD: ACCELERATION FUNDING**

In 2017, Dr. Bottini and his Harrington Therapeutics Development advisors applied for additional funds for his project, beyond the Stage 1 grant funds. The Harrington Investment Advisory Board evaluated and selected his project for a Stage 2 acceleration award designed to optimize the project for commercial partnering, specifically addressing process development, safety and pharmacology studies.



# CHALLENGING THE STATUS QUO IN THE FIGHT AGAINST ALZHEIMER'S DISEASE

For Paul and Cathy Douglas, Alzheimer's is personal. Having family members affected by the debilitating disease, the couple from British Columbia, Canada knew they wanted to join the fight against it. Alzheimer's disease (AD), the most common cause of dementia, crosses all demographics and is indiscriminate in the damage it does to patients and their families. Currently, there is no cure or treatment to reverse AD, and an estimated 500,000 new cases will be diagnosed in the US this year.

Despite the near ubiquity of AD and billions spent annually to find a cure, there is a shocking lack of innovation and promising treatments. Paul and Cathy Douglas were drawn to Harrington Discovery Institute because of frustrations they share with the countless people and families who are demanding action.

For decades, AD research has focused predominantly on ways to reduce beta-amyloid plaques and tau tangles in the brain, which were the defining features of AD when it was discovered over a century ago. But these efforts have had very limited success. There are other promising pathways for therapy in AD, however, such as the various efforts being implemented by Harrington-supported scholars. Paul and Cathy Douglas saw this as an opportunity.

The Douglasses are highly active and widely respected leaders in their Canadian community, with a strong history of impact philanthropy. Paul serves as Chairman of the board of PCL Construction Inc., the largest general contracting construction company in Canada, and previously led PCL as President and Chief Executive Officer until 2016. After meeting with leaders at Harrington

Discovery Institute, Paul and Cathy were immediately interested in its network of scientists and portfolio approach to drug development. By developing medicines that protect neuronal synapses from degradation in AD, for example, or that optimize function of a neurotransmitter that is significantly diminished in the brains of people with AD, Harrington Scholars are providing 'multiple shots on goal' outside of the traditional approaches in the field. The Douglas family recognized this as a way to maximize the impact of their philanthropy.

"Alzheimer's is one of the greatest public health challenges of our generation. Recognizing the scale of the problem, we knew we needed to be strategic about our giving and find a unique lane that we could embrace. We were impressed by Harrington's disciplined processes and

**55 MILLION**  
PEOPLE WORLDWIDE ARE LIVING WITH ALZHEIMER'S OR OTHER DEMENTIAS

**500,000**  
NEW CASES OF ALZHEIMER'S DISEASE WILL BE DIAGNOSED THIS YEAR

**\$321 BILLION**  
IS THE COST OF CARE FOR AMERICANS AGE 65+ WITH ALZHEIMER'S OR OTHER DEMENTIAS





*“Our hope is that our contribution encourages others to join the fight against Alzheimer’s disease by supporting diverse new treatments that are actively in development by the network of outstanding scientists being supported by the Harrington Discovery Institute Center for Brain Health Medicines. We all are working towards the same goal. We simply can’t wait”*

**CATHY AND PAUL DOUGLAS**

procedures that are rapidly transforming research into solutions and medicines faster than anything we have seen elsewhere. We have no time to waste when it comes to cures and prevention of Alzheimer’s disease,” said Paul.

“I was intrigued by the science. In talking to the team at Harrington, I could see that the scholars they support represent the best of the best. Their funded projects show great promise and need critical funding, and more importantly the drug development expertise and guidance offered by the Harrington Discovery Institute. This will allow them to advance their discoveries into human clinical trials and eventually into new medicines,” said Cathy.

The Paul and Cathy Douglas Scholars in Alzheimer’s disease will be launched in 2023. Douglas Scholars will receive comprehensive drug development support and funding where they will work closely with Harrington therapeutic development advisors to advance their treatments towards patients.

“We saw an opportunity to create the most impact in a relatively short time because, like so many people and families, we are waiting anxiously for a cure and new therapies that are desperately needed,” Paul added.

## **DEMENTIA: THE GREAT UNMET NEED OF OUR TIME**



**ANDREW A. PIEPER, MD, PhD**

Director, Center for Brain Health Medicines  
at Harrington Discovery Institute  
Director, Translational Therapeutics Core of the  
Cleveland Alzheimer’s Disease Research Center  
Rebecca E. Barchas, MD, Professor in Translational  
Psychiatry at Case Western Reserve University  
Morley Mather Chair in Neuropsychiatry at  
University Hospitals

Alzheimer’s disease is the most common form of dementia worldwide, and causes loss of cognitive function that steadily and progressively impairs all aspects of normal daily living. Its impact is devastating for families and communities. Despite its discovery well over a century ago, there are still no effective treatments for patients with Alzheimer’s disease.

Combating this major unmet need requires innovative approaches to discovery and development of new medicines that will prevent, slow, halt, or reverse the disease. At the Center for Brain Health Medicines at Harrington Discovery Institute, we are pursuing this goal through our scholar pipeline to attack the disease from multiple angles, focusing specifically on projects with potential to enter into formal clinical development within 1–2 years.

I invite you to learn more about the breakthrough discoveries we are helping advance into medicines by visiting

**[HarringtonDiscovery.org/BrainHealthMedicines](https://HarringtonDiscovery.org/BrainHealthMedicines)**.



# 2022 SCIENTIFIC SYMPOSIUM



## CONVENING FOR CURES

The 9th Annual Harrington Scientific Symposium was held May 25-26, 2022 with speakers and audience members from around the globe. More than 300 attendees participated in the two-day virtual event.

“We now have a diverse portfolio of discoveries, a financing continuum that spans from philanthropy to venture-investments, greatly improved scholar opportunities and funders and donors who consider our model differentiated and meaningful,” said **Jonathan S. Stamler, MD**, President and Co-Founder, Harrington Discovery Institute, during the Symposium’s opening remarks.

**Seth Field, MD, PhD**, Investigator and Director of Physician-Scientist Programs at Harrington Discovery Institute, served as emcee for the event, introducing

speakers and moderating scientific presentations from Harrington Scholars.

Harrington Project founder **Ronald G. Harrington** welcomed attendees and reflected on Harrington Discovery Institute’s ability to attract high quality, high-performing partners throughout its ten-year journey.

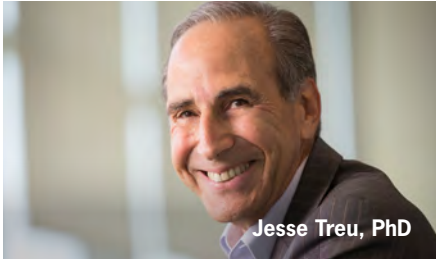
Other speakers included global leaders in science, medicine and drug development. **Jeffrey Leiden, MD, PhD, Executive Chairman, Vertex Pharmaceuticals**, delivered the Keynote Address, Discovering Transformative Medicines: The Vertex Innovation Model.

The co-recipients of the 2022 Harrington Prize, **James Crowe, Jr., MD, Vanderbilt University** and **Michel Nussenzweig, MD,**

**PhD, The Rockefeller University**, (See pages 12-13), presented their breakthrough innovations in the use of human antibodies to treat COVID-19.

The audience also heard from two highly accomplished physician-scientists on their Harrington Scholar experience. **Rosa Bacchetta, MD, Stanford University**, spoke about her novel gene therapy for the rare autoimmune disease, IPEX Syndrome, which received FDA approval to test in a Phase 1 clinical trial. **Marc Wein, MD, PhD, Massachusetts General Hospital**, shared his breakthrough work on orally-available salt inducible kinase (SIK) inhibitors, a new drug class for the treatment of osteoporosis, which was licensed to Radius Health.

**Andrew Pieper, MD, PhD**, Investigator and Director of Harrington’s Brain Health Medicines



Jesse Treu, PhD



Jerri Rook, PhD



John Rice, PhD



Stephen Strittmatter, MD, PhD



Graeme Martin, PhD



Nabil Alkayed, MD, PhD

Center, moderated a panel showcasing breakthrough work in the prevention and treatment of Alzheimer’s disease. The panel featured **Dr. Jerri Rook from Vanderbilt University** (2015 ADDF-Harrington Scholar), **Dr. Stephen Strittmatter of Yale University** (2020 Harrington Scholar-Innovator), and **Harrington Discovery Institute Investigator and President Dr. Jonathan Stamler**. Dr. Pieper introduced the new Brain Health Medicines Scholar program in Alzheimer’s disease and its first funded Vinney Scholar, **Dr. Nabil Alkayed, from Oregon Health & Science University** (See page 45).

The role of Harrington’s Investment Advisory Board (IAB) was highlighted in a panel, *Creating a Value Proposition that Attracts Investment*. IAB members **Drs. John Rice, Graeme Martin and Jesse Treu** shared their perspective on how Scholars can create a compelling value proposition and meet critical milestones that, in turn, attract industry interest and additional funding.



**Harrington  
Discovery  
Institute**



*“I loved learning about the impressive work conducted by my fellow scholars, and I appreciated the critical, insightful input from the scientific advisors.”*

**JENNIFER CHEN, MD**

Assistant Professor, Medicine  
University of California, San Francisco  
2021 Harrington Scholar-Innovator

*Thank you!*  
**TO OUR 2022  
PANEL MEMBERS**

**SCIENTIFIC ADVISORY BOARD**

- David Ginsburg, MD
- Barbara B. Kahn, MD
- Andrew Marks, MD
- Michael Welsh, MD

**THERAPEUTICS  
DEVELOPMENT CENTER**

- Jim Bryson, PhD
- Bill Murray, PhD
- Larry Olanoff, MD, PhD
- George Trainor, PhD

**SAVE THE DATES:**



**MAY 22-23, 2024**

**MAY 21-22, 2025**



FOR MORE INFORMATION:  
[HarringtonDiscovery.org/Events](https://HarringtonDiscovery.org/Events)

## HARRINGTON SCHOLARS 2013–2023

### MAJOR DISEASES

#### 2023 HARRINGTON SCHOLAR-INNOVATORS

**KIRK CAMPBELL, MD**  
Icahn School of Medicine  
at Mount Sinai

**JACQUES GALIPEAU, MD**  
University of Wisconsin – Madison

**WON JIN HO, MD**  
Johns Hopkins University

**MAXIMILLIAN KONIG, MD**  
Johns Hopkins University

**BERGE MINASSIAN, MD**  
UT Southwestern

**MICHAEL PACOLD, MD, PhD**  
New York University

**ANTHONY ROSENZWEIG, MD**  
University of Michigan

**JEFFREY SCHELLING, MD**  
Case Western Reserve University

**MING-RU WU, MD, PhD**  
Dana-Farber Cancer Institute

**TIMOTHY YU, MD, PhD**  
Boston Children's Hospital

#### 2022 HARRINGTON SCHOLAR-INNOVATORS

**BURTON DICKEY, MD**  
MD Anderson Cancer Center

**DIANA FARMER, MD**  
University of California, Davis

**JAMES HAGOOD, MD**  
University of North Carolina  
at Chapel Hill

**LI LAN, MD, PhD**  
Massachusetts General Hospital

**CAROLYN LEE, MD, PhD**  
Stanford University

**MICHAEL LIN, MD, PhD**  
Stanford University

**FRANCIS MCCORMACK, MD**  
University of Cincinnati

**DAVID MYUNG, MD, PhD**  
Stanford University

**BERND SCHNABL, MD**  
University of California, San Diego

**LOREN WALENSKY, MD, PhD**  
Dana-Farber Cancer Institute

**HANS-GUIDO WENDEL, MD**  
Memorial Sloan Kettering  
Cancer Center

#### 2021 HARRINGTON SCHOLAR-INNOVATORS

**JENNIFER CHEN, MD**  
University of California,  
San Francisco

**JOHN CHORBA, MD**  
University of California,  
San Francisco

**JOSEPH CONTESSA, MD, PhD**  
Yale University

**TOREN FINKEL, MD, PhD**  
University of Pittsburgh

**MARIA GRAZIA  
RONCAROLO, MD**  
Stanford University

**AARON SCHIMMER, MD**  
University of Toronto

**JILL SMITH, MD**  
Georgetown University

**XINNAN WANG, MD, PhD**  
Stanford University

#### 2020 HARRINGTON SCHOLAR-INNOVATORS

**RIZWAN HAQ, MD, PhD**  
Dana-Farber Cancer Institute

**MICHAEL HOLTZMAN, MD**  
Washington University

**KYU RHEE, MD, PhD**  
Weill Cornell Medicine

**STEPHEN STRITTMATTER,  
MD, PhD**  
Yale University

**DONALD WEAVER, MD,  
PhD, FRCPC, FCAHS**  
University Health Network

**TIMOTHY YU, MD, PhD**  
Boston Children's Hospital

#### 2019 HARRINGTON SCHOLAR-INNOVATORS

**ROBERT E. ANDERSON, MD, PhD**  
University of Oklahoma

**ROSA BACCHETTA, MD**  
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**  
Johns Hopkins University

**ELLEN YEH, 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



FOR MORE INFORMATION:  
[HarringtonDiscovery.org/Scholars](https://HarringtonDiscovery.org/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**  
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

**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. COLLIER, MD**  
The Rockefeller University

**XIANXIN HUA, MD, PhD**  
University of Pennsylvania

**RICHARD J. JOHNSON, MD**  
University of Colorado

**MARIKKI LAIHO, MD, PhD**  
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

**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**  
Johns Hopkins University

**LARRY S. SCHLESINGER, MD**  
\*The Ohio State University

**ROBERT B. WILSON, MD, PhD**  
University of Pennsylvania

**2023 HARRINGTON-MSTP  
SCHOLAR**

**JENNINGS LUU**  
Case Western Reserve University

**2022 HARRINGTON-MSTP  
SCHOLAR**

**WILLIAM WULFTANGE**  
Case Western Reserve University

**2021 HARRINGTON-MSTP  
SCHOLAR**

**DEREK WONG**  
Case Western Reserve University



## HARRINGTON SCHOLARS 2013–2023

### 2020 HARRINGTON-MSTP SCHOLAR

YI FAN CHEN  
Case Western Reserve 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

### BRAIN HEALTH MEDICINES

### 2022 ADDF-HARRINGTON SCHOLARS

DONALD WEAVER, MD,  
PhD, FRCPC, FCAHS  
University Health Network

PAUL TESAR, PhD  
Case Western Reserve University

### 2021 ADDF-HARRINGTON SCHOLAR

CHRISTIANE WRANN, DVM, PhD  
Massachusetts General Hospital

### 2020 ADDF-HARRINGTON SCHOLARS

PAUL FISH, PhD  
University College London

PAUL WORLEY, MD  
Johns Hopkins University

### 2019 ADDF-HARRINGTON SCHOLAR

EUGENIA TRUSHINA, PhD  
Mayo Clinic

### 2018 ADDF-HARRINGTON SCHOLAR

KEVIN HODGETTS, PhD  
Brigham & Women's Hospital

### 2017 ADDF-HARRINGTON SCHOLAR

DIANNE M. PEREZ, PhD  
Cleveland Clinic  
Lerner Research Institute

### 2016 ADDF-HARRINGTON SCHOLARS

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

### 2022 VINNEY SCHOLARS

NABIL ALKAYED, MD, PhD  
Oregon Health and Science  
University

XIN QI, PhD  
Case Western Reserve University

### 2019 GUND HARRINGTON SCHOLAR

STEPHEN MARTIN, PhD  
University of Texas at Austin

### 2018 GUND HARRINGTON SCHOLARS

ZHENG-RONG LU, PhD  
Case Western Reserve University

KRISHANU SAHA, PhD  
University of Wisconsin-Madison

### 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  
Johns Hopkins University



FOR MORE INFORMATION:  
[HarringtonDiscovery.org/Scholars](https://HarringtonDiscovery.org/Scholars)

## RARE DISEASES

### 2021 HARRINGTON UK RARE DISEASE SCHOLARS

**PIETRO FRATTA, MD, PhD**  
University College London

**ANGELA RUSSELL, DPhil**  
University of Oxford

**HELEN WALLER-EVANS, DPhil**  
Cardiff University

**WYATT YUE, PhD**  
\*University of Oxford

**HAIYAN ZHOU, MD, PhD**  
University College London

### 2018 HARRINGTON RARE DISEASE SCHOLARS

**ED GRABCZYK, PhD**  
LSU Health Sciences Center  
in New Orleans

**XIANXIN HUA, MD, PhD**  
University of Pennsylvania

**JUSTIN ICHIDA, PhD**  
University of Southern California

**JEANNIE LEE, MD, PhD**  
Massachusetts General Hospital

**JOHN MARSHALL, PhD**  
Brown University

**XIN QI, PhD**  
Case Western Reserve University

**DANIEL R. SCOLES, PhD**  
University of Utah

**JAMES A. SHAYMAN, MD**  
University of Michigan

## COVID-19

### 2020 HARRINGTON SCHOLARS FOR CORONAVIRUS

**MICHAEL BARRY, PhD**  
Mayo Clinic

**KATHERINE FITZGERALD, PhD**  
University of Massachusetts

**BENJAMIN GASTON, MD**  
Indiana University

**JEFFREY S. GLENN, MD, PhD**  
Stanford University

**ANASTASIA KHVOROVA, PhD**  
University of Massachusetts

**YULIA KOMAROVA, PhD**  
University of Illinois

**ANNE MOSCONA, MD**  
Columbia University

**MICHEL NUSSENZWEIG, MD, PhD**  
The Rockefeller University

**JAMES REYNOLDS, PhD**  
University Hospitals of Cleveland/  
Case Western Reserve University

**JOSEPH VINETZ, MD**  
Yale University

**JAMES WELLS, PhD**  
University of California,  
San Francisco

**JAMES WILSON, MD, PhD**  
University of Pennsylvania

## IN MEMORIAM

**CLARK W. DISTELHORST, MD**  
2015 Harrington Scholar-Innovator  
Case Western Reserve University

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

# Harrington Discovery Institute

 University Hospitals | Cleveland, Ohio

11407 Euclid Avenue  
2nd Floor  
Cleveland, OH 44106  
USA



## OUR MISSION:

To accelerate promising discoveries  
into medicines for unmet needs

