When COVID-19 hit, our team took immediate action. We created a call for medical breakthroughs for broad-spectrum anti-COVID drugs and next-generation vaccines that would aid in this pandemic and avert future ones. Within weeks, we received nearly 300 applications from academic medical centers in the US, UK and Canada, identified 50 medicines with great promise, and funded the first 12.

This epitomizes the Harrington Discovery Institute (HDI) values of urgency, creativity and excellence, and of doing right. Because of this, we now have among the world’s largest portfolio of pandemic-related, breakthrough innovations.

Our strategy and culture are differentiated, special, and effective. Take our novel partnership with Morgan Stanley Philanthropy Management to create an innovation platform for high-net-worth clients, helping them to learn about latest treatments. The donations the clients make advance the discoveries of our innovators into new treatments. We believe Morgan Stanley GIFT Cures powered by Harrington Discovery Institute will markedly accelerate successes in academic drug discovery and development.

In 2020 we also launched a new capital raising strategy through which we are able to make investments in early stage drug discovery toward the goal of new cures. The returns from such investments come back to HDI for further HDI activities, creating a virtuous cycle of investment profits flowing to our charitable mission. The new Advent-Harrington Impact Fund utilizes the Morgan Stanley Impact Investing platform in partnership with Advent Life Sciences, a leading transatlantic venture investor focused on life sciences. HDI not only receives returns on its investments but also benefits from rights it has to a share of the carried interest.

Further, we deepened our partnership with the University of Oxford, to create a global rare disease center, and we successfully launched a UK-wide grants program. We are a powerful participant in one of the greater unmet needs of our time—finding treatments and cures for some of the world’s 7,000 known rare diseases.

All of these accomplishments rest on the foundational fact that we have funded more than 130 scholars from 58 institutions and they have made incredible progress. I’ll highlight one of 29 HDI scholars to start a new company—Jerri Rook, a 2015 ADDF-Harrington Scholar; her Alzheimer’s discovery was recently licensed by pharma for up-to-$500 million; it continues to progress well into Phase 2 clinical trials!

We have a long way to go in our work. I think all of us at Harrington Discovery Institute sometimes feel like we are in Robert Frost’s famous poem—namely, that we have miles to go before we sleep. Yet, we take heart in knowing we are tangibly and significantly improving the drug discovery landscape for the benefit of patients and society.

Sincerely,

JONATHAN S. STAMLER, MD
President, Harrington Discovery Institute, University Hospitals Health System
Robert S. and Sylvia K. Reitman Family Foundation Distinguished Chair of Cardiovascular Innovation, UH Cleveland Medical Center and Case Western Reserve University Professor of Medicine and of Biochemistry and Director, Institute for Transformative Molecular Medicine, Case Western Reserve University School of Medicine
NO ONE TRAINS YOU TO BE IN DRUG DISCOVERY. Without Harrington we’d be at a big disadvantage.”

Harrington is always asking, “How best can we COMMERCIALIZE THE POTENTIAL of this discovery?”

The Harrington Discovery Institute CLEARLY FILLS THE GAPS in what an academic technology development office can do to help develop new medicines.”

The Harrington Discovery Institute is amazing. EXACTLY WHAT THE WORLD NEEDS.”
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-3</td>
<td>A letter from Jonathan S. Stamler, MD President, Harrington Discovery Institute</td>
</tr>
<tr>
<td>4</td>
<td>From Our Scholars</td>
</tr>
<tr>
<td>6-7</td>
<td>Growing Our Transatlantic Innovation Network</td>
</tr>
<tr>
<td>8</td>
<td>Talk About Acceleration! Ronald G. Harrington Entrepreneur and Philanthropist</td>
</tr>
<tr>
<td>9</td>
<td>Paving the Way for Medical Philanthropists Melanie Schnoll Begun Morgan Stanley</td>
</tr>
<tr>
<td>10-15</td>
<td>Where World-Class Drug Development Meets World-Class Science Oxford-Harrington Rare Disease Centre</td>
</tr>
<tr>
<td>16-17</td>
<td>Applying Brilliant Science to Orphan Diseases Atul Chopra, MD, PhD Harrington Investigator</td>
</tr>
<tr>
<td>18-19</td>
<td>COVID-19 Rapid Response Initiative</td>
</tr>
<tr>
<td>22-23</td>
<td>Harrington Scholar Programs</td>
</tr>
<tr>
<td>24</td>
<td>Announcing the 2020 Scholars</td>
</tr>
<tr>
<td>25</td>
<td>Meet Our 2018 and 2019 Scholars</td>
</tr>
<tr>
<td>26-27</td>
<td>2019 HARRINGTON SCHOLAR-INNOVATORS Robert Anderson, MD, PhD Rosa Bacchetta, MD Gerald Dorn, II, MD Joachim Herz, MD Paul Hruz, MD, PhD V. Vinood Mothia, MD Dawn Wetzel, MD, PhD T.C. Wu, MD, PhD Ellen Yeh, MD, PhD</td>
</tr>
<tr>
<td>28-29</td>
<td>2018 AND 2019 ADDF-HARRINGTON SCHOLARS Kevin Hodgetts, PhD Eugenia Trushina, PhD</td>
</tr>
<tr>
<td>30-31</td>
<td>2019 GUND-HARRINGTON SCHOLAR Stephen Martin, PhD</td>
</tr>
<tr>
<td>32-33</td>
<td>2018 HARRINGTON RARE DISEASE SCHOLARS Ed Grabczyk, PhD Xianxin Hua, MD, PhD Justin Ichida, PhD Jeannie Lee, MD, PhD John Marshall, PhD Xin Qi, PhD Daniel Scoles, PhD James Shayman, MD</td>
</tr>
<tr>
<td>34-35</td>
<td>The Harrington Advantage</td>
</tr>
<tr>
<td>36-37</td>
<td>The Team at the Core of the Harrington Project Mission Diana R. Wetmore, PhD</td>
</tr>
<tr>
<td>38-39</td>
<td>Partnering with Acadamia Q&amp;A Marisa Naughton, MBA</td>
</tr>
<tr>
<td>40-41</td>
<td>Jeffrey Glenn Scholar Case Study: Assembling a Virtual Pharma Team to Fight Influenza</td>
</tr>
<tr>
<td>42-43</td>
<td>Maximizing Impact from Philanthropic Funds John Rice, PhD</td>
</tr>
<tr>
<td>44-45</td>
<td>Balancing Risk and Reward in Drug Development Satish Jindal, PhD BioMotiv</td>
</tr>
<tr>
<td>46-47</td>
<td>Fighting Diseases is in the Cleveland Foundation’s DNA</td>
</tr>
<tr>
<td>48-49</td>
<td>Rare Disease Day Event</td>
</tr>
<tr>
<td>50-51</td>
<td>2019 Scientific Symposium</td>
</tr>
<tr>
<td>52-53</td>
<td>Harrington Scholars 2013-2020</td>
</tr>
</tbody>
</table>
In February 2019, Ron and Nancy Harrington traveled to the UK to celebrate the launch of the Oxford-Harrington Rare Disease Centre. With 250 scientists working on rare diseases, the Oxford Rare Disease Initiative has world-renowned capabilities. The new center brought Harrington Discovery Institute (HDI) beyond North America, making it an international, transatlantic drug development organization.

“It was amazing!” says Mr. Harrington. “Nancy and I loved being around incredible scientists working to help save thousands of lives. We knew this was the genesis of an innovative and effective relationship.”

When they funded the Harrington Discovery Institute in 2012, the Harrington family was on the leading edge of medical philanthropy, a sector that is increasingly central to success in drug development and global health. Because of its foresight, HDI is catalyzing change at the highest levels in medicine and philanthropy. Take the partnership it forged with Morgan Stanley Global Impact Funding Trust (GIFT) in 2019 to create Morgan Stanley GIFT Cures powered by Harrington Discovery Institute. Mr. Harrington is thrilled that the iconic financial institution is co-leading the medical philanthropy charge.

Referring to Melanie Schnoll Begun, head of Morgan Stanley Philanthropy Management, he says. “I quickly knew she had the perceptiveness to see how important the unmet need for new therapeutics is and she had the tenacity to champion it throughout Morgan Stanley. We couldn’t have picked a better partner.”

Through Morgan Stanley GIFT Cures, wealth advisors introduce their clients to an exclusive community of philanthropists, foundations, companies, and family offices that share a common goal of eradicating disease. The donations are granted by Harrington Discovery Institute to its network of scientists making discoveries. But as fast as medical philanthropy is growing, medical needs are also growing.

“We’re excited that Harrington Discovery Institute is pursuing multiple innovative strategies to raise capital for HDI to further expand its ability to meet the needs of patients. For example, the strategy being implemented with Advent Life Sciences on the Morgan Stanley platform is very promising. We believe the involvement of an early-stage life sciences venture capital fund will enable innovators to advance drug discoveries further down the commercialization pipeline, generate more wins, and save more lives. There are no pharma-type funds the size HDI is aiming for with its novel strategies,” Mr. Harrington says.

Mr. Harrington and his family see the Harrington Discovery Institute response to COVID-19 as a perfect example of why the Institute has a bright future. “The pandemic has forced an even greater sense of urgency,” he says. Within weeks of the surge at North American hospitals, the Institute had issued a call for proposals for COVID-19 treatments. The team received nearly 300 proposals from 122 academic institutions, identified 50 high-priority therapies, and announced 12 winners.
In 2017, Morgan Stanley Philanthropy Management was searching for opportunities to address the reality that cures exist for only five percent of known diseases. Its clients were telling the firm that they were passionate about medical philanthropy and wanted to give more in that area. Leading the philanthropy arm of the client-driven firm, Ms. Schnoll Begun and her team knew they needed to deliver, and they sought institutions paving the way. After meeting with Harrington Discovery Institute leadership, Ms. Schnoll Begun knew she had found the answer, and she led the launch of Morgan Stanley GIFT (Global Impact Funding Trust) Cures powered by Harrington Discovery Institute.

Ms. Schnoll Begun reflects, “Harrington Discovery Institute has the right combination of philanthropy, pharma, and investing. Its ability to accelerate the drug development process by ensuring that the world’s best discoveries turn into next-generation medicines and fill unmet needs made it the ideal partner.”

For instance, Morgan Stanley clients who have experience with rare diseases have long found themselves without hope because of the paucity of scientists working in—and lack of financial resources entering into—the space. She says, “The Harrington Discovery Institute partnership with Oxford offers tremendous hope. It brings the best science and critical funding to clinical areas that are not research priorities for governments, industry, funders, or charities. Our clients want to participate in medical philanthropy by seeing their resources speed up drug development and get cures to patients.”

She also cites, as an example of making medical philanthropy topical, big, and effective, the Institute’s response to COVID-19. “Harrington Discovery Institute rapidly responded to the global pandemic, which our clients and we see as the great unmet need of our time. It quickly developed one of the world’s largest portfolios of discoveries, including next-generation vaccines that may target new strains of the virus.” She went on to explain that the pandemic has made philanthropists realize more than ever the need to play an active role today to improve health tomorrow.

Harrington Discovery Institute is proud to partner with Morgan Stanley and visionaries like Ms. Schnoll Begun who together are enabling growing numbers of medical philanthropists to accelerate new medicines.

**PAVING THE WAY**

**FOR MEDICAL PHILANTHROPISTS**

**MELANIE SCHNOLL BEGUN**

Managing Director, Head of Philanthropy Management
President, Morgan Stanley GIFT
TRANSATLANTIC PARTNERSHIP

OXFORD-HARRINGTON RARE DISEASE CENTRE
Where World-Class Drug Development Meets World-Class Science

Approximately 350 million people worldwide are living with a rare disease, and half of them are children. With more than 7,000 known rare diseases, and only five percent having an approved treatment, rare disease represents one of the greatest unmet needs in healthcare today.

The Oxford-Harrington Rare Disease Centre (OHC) was established in early 2019 to bring together the capabilities, resources, and expertise of the University of Oxford and Harrington Discovery Institute to develop new rare disease treatments, for which therapeutic options are severely lacking.

"Imagine receiving the devastating news that your child or loved one has a rare disease. It may have taken years to get to an accurate diagnosis, and your journey to finding a suitable treatment is just beginning," says Dr. Mukesh Jain, OHC Co-Director and Chief Scientific Officer of Harrington Discovery Institute. "Improving outcomes for those with a rare disease requires a bold, synergistic approach. One that engages the best and brightest scientists and creates a clear pathway to clinical trials."

The work of the OHC supports the drug development life cycle from early drug discovery to preclinical studies, clinical development, regulatory approval and ultimately through to commercialization.

"This affiliation represents a commitment to patients first and a tremendous opportunity to improve the health and outcomes of those living with a rare disease."

JONATHAN S. STAMLER, MD
President, Harrington Discovery Institute

Identifying Key Themes

The OHC will focus primarily on rare diseases that have a clear genetic basis and present early in life. Research programs fall under three translational research themes:

• Neurological disorders
• Developmental disorders
• Cancer

Programs will leverage the key strengths of both partners, and may include rare diseases that fall outside of these themes.

Our partnership with Harrington Discovery Institute recognizes the combined experience needed in world-class science and drug development if we are to change the rare disease landscape in a meaningful way."

SIR JOHN BELL
Regius Professor of Medicine, University of Oxford

A Transformational Opportunity

In an unprecedented development partnership, Morgan Stanley GIFT Cures, the University of Oxford, Harrington Discovery Institute and University Hospitals are working together to scale the impact of the Oxford-Harrington Rare Disease Centre. This affiliation is a commitment to patients first and a tremendous opportunity to improve the health and outcomes of those living with a rare disease. To learn more, contact HDIDevelopment@HarringtonDiscovery.org.
Oxford-Harrington Rare Disease Centre

**BUILDING AN INTEGRATED STRATEGY**

OHC activities fall into two groupings—intramural and extramural—which work together in a complementary manner to achieve its mission. Intramural activities include the appointment of core faculty members both in the UK and in the US, who will collaborate on common problems while conducting their own rare disease research. Extramural activities include the sourcing of new research projects through competitive calls for proposals where projects and investigators are selected and supported with funding and drug discovery advisory services.

**PRESENTING A COMPELLING CASE**

“With the expertise that Harrington brings in, they help us decide which bits to translate, efficiently and cost-effectively. Their Therapeutics Development team has vast experience in guiding scientists through pre-clinical phases, enabling us to present a much more compelling case to pharma or those who give philanthropically. It’s a much more comprehensive way of doing the work,” says Professor Wood. Indeed, he reports that many entities are more eager than ever to work with Oxford. “Every partner we’ve spoken to likes what we’ve put together with Harrington.”

Professor Wood credits the Harrington ethos as a primary reason the working relationship is so strong. “Harrington has done an unusual thing—they see no need to build everything in Cleveland, but rather they have taken the opposite approach,” he says. “Their projects can be anywhere, and they have relationships with investigators and institutions all over the US, and now the UK.”

**GROWING THE CENTRE**

Essential to the growth of the OHC is the integration of partners and philanthropy. Partnerships with pharma companies, foundations, US and UK governments, and institutions such as global financial services powerhouse Morgan Stanley, will help fund the pipeline of drug development projects created.

Families of individuals with a rare disease will be engaged through impact philanthropy, where they will have the opportunity to work directly with the OHC to shape research and innovation.

**A PARTNERSHIP PRIMED FOR SUCCESS**

“The partnership has a genuine collaborative outward-looking mentality, which is very healthy and very attractive to those of us at Oxford and in the UK,” says Professor Wood. “We foresee the day when a patient with a rare disease, or the parents of a child born with one, will turn first to our center for answers,” says Dr. Jain. “In addition, as the OHC and its successes become more widely known, we will strive to provide something else for patients and their families, and that is, hope.”

**OUR VISION**

To be the global leader in eliminating rare diseases.

**OUR MISSION**

To advance scientific discovery into novel medicines for patients suffering from rare diseases.

---

**PROFESSOR GEORG HOLLÄNDER**
Head of the Department of Paediatrics, University of Oxford

“Our Centre promises to advance the best scientific breakthroughs not only at Oxford but also across the UK. This is a unique feature of our commitment to science and patients and one I am most proud of,” said Professor Georg Holländer, Head of the Department of Paediatrics, University of Oxford.

**PROFESSOR MATTHEW WOOD, PhD**
Director, Oxford-Harrington Rare Disease Centre Investigator, Harrington Discovery Institute Professor of Neuroscience, University of Oxford

**MUKEISH K. JAIN, MD**
Co-Director, Oxford-Harrington Rare Disease Centre Chief Scientific Officer, Harrington Discovery Institute Visiting Professor, University of Oxford
In 2018, when Dr. Atul Chopra joined the Harrington Discovery Institute as a Harrington Investigator and Associate Director of the Harrington Rare Disease Program, it was a testament to the potential efficacy and impact of the Institute’s platform.

Dr. Chopra was the Caroline Wiess Law Scholar and Assistant Professor in Molecular and Human Genetics and Molecular and Cellular Biology at the Baylor College of Medicine in Houston. There, he and his team were searching for answers for patients with neonatal progeroid syndrome, a rare genetic condition of extreme leanness, among other symptoms. This work led to the 2016 discovery of a hormone named asprosin that regulates appetite and glucose levels, and potentially opened the door to a novel treatment for metabolic syndrome.

Dr. Chopra was doing breakthrough work at a prestigious institution. But the unique model of the Harrington Discovery Institute presented opportunities he found difficult to resist.

“Most academic institutions are doing discovery, but not drug development,” Dr. Chopra says. “Part of my own mission is to develop drugs based upon discoveries I make, and generally speaking, that’s not something that academia is set up to do. Like most academic researchers, I really didn’t know anything about how to take a discovery and convert it to a drug; I didn’t know much about how the pipeline works. That process is precisely what Harrington was established to do.”

Dr. Chopra was also drawn to how Harrington is dedicated to physician-scientists, who treat patients as well as work in a lab. “Folks here speak my language—they understand the demands and opportunities unique to physician-scientists,” he says.

In 2018, as the Harrington Discovery Institute was establishing a relationship with the University of Oxford with the goal of creating the Oxford-Harrington Rare Disease Centre (OHC), the addition of Dr. Chopra made perfect sense. The OHC brings together the capabilities, resources and expertise of both institutions to deliver new rare disease treatments, for which therapeutic options are lacking. The OHC will set the science and innovation agenda to support cutting-edge rare disease breakthroughs across the UK and US with the greatest chance for clinical impact.
After finding that asprosin deficiency due to their genetic mutations led to remarkably low appetite and body weight in neonatal progeroid syndrome patients, Dr. Chopra went on to show that obese people have high blood asprosin levels. Therefore, a therapy that dampens the effect of asprosin could lead to less eating and weight loss in those with obesity, one of the most common human conditions. Dr. Chopra has tested this idea in preclinical studies with promising results.

A classic example of how studying rare diseases can benefit common diseases is the case of Nobel Prize-winning Drs. Brown and Goldstein, University of Texas Southwestern researchers who studied a disease that causes high cholesterol called familial hypercholesterolemia, the severe variant of which is rare. Their research revealed that cells have receptors that regulate the amount of cholesterol-containing particles circulating in the blood stream. That led to the development of cholesterol-lowering statin drugs, now one of the most widely prescribed medications in the world.

Other examples of the connection between rare disease research and common diseases:

- Much of what is known about the genetic basis for migraines comes from studies on the rare familial hemiplegic migraine disease.
- Work done on the rare genetic disease Fanconi anemia has led to improved techniques for prenatal diagnosis of early childhood cancers.
- Patients with the rare Gaucher disease are at increased risk for Parkinson's disease. By studying Gaucher, there is the potential to identify pathways, genes and therapies that might be involved in or affect Parkinson's and related disorders.
- Once researchers better understand the genetic pathway of an extremely rare neurological disease called Type II congenital disorders of glycosylation, that could be relevant to the study of viruses that cause Zika, Ebola and the common cold.

Studying rare diseases is critical to understanding medicine and biology, and can lead to novel treatments for common diseases. This is an important tenet in Harrington Discovery Institute’s commitment to addressing unmet needs in patient care across diseases.
In April 2020, Harrington Discovery launched a major initiative to galvanize its transatlantic network of academic institutions, foundations, and philanthropic partners to respond to the global coronavirus pandemic. By June, it had built one of the world’s largest portfolios of breakthrough COVID-19 therapies.

Accelerating programs in its current portfolio that may target coronavirus, and issuing a transatlantic call for proposals, Harrington Discovery Institute yielded nearly 300 proposals from 122 academic institutions in North America and the UK. In further action, the Institute is raising capital to resource this effort through Morgan Stanley GIFT Cures, its philanthropic partnership with Morgan Stanley.

See page 24 for a list of Harrington Scholars for Coronavirus.

JOIN THE FIGHT AGAINST COVID-19
Morgan Stanley GIFT Cures powered by Harrington Discovery Institute is raising $100 million from philanthropists to advance promising treatments for COVID-19, as well as new medicines to avert future pandemics.

To learn more, please contact HDIDevelopment@HarringtonDiscovery.org.
How fortunate for humanity that there are scientific investigators. Typically researching for years without their discoveries manifesting in anything directly useful to the public, their boundless perseverance astonishes the layperson. The force that motivates them is a lively curiosity, a thirst to penetrate the unknown, to solve mysteries, to find what has not been found.

For Dr. Carl June, curiosity was sparked in childhood by his mother’s lupus, with its classic symptoms like rashes, sun sensitivity, fatigue. Watching her body fight and overcome the inflammatory disease, he became intrigued by the capabilities of the immune system.

Dr. June began as a physician in oncology, studying the emerging therapy of bone marrow transplantation, followed by a decade as an HIV researcher in a Navy-funded lab. There, he developed a technique to boost immune function in HIV patients by modifying their T cells, whose role in the body is to inspect cells, call for reinforcements when necessary, and kill HIV-infected cells. (During this period Dr. June also demonstrated the critical role of the CD28 receptor in T cell activation and growth, which led to a therapy that was approved by the FDA for the treatment of rheumatoid arthritis.)

In 1999, Dr. June moved his lab to the University of Pennsylvania, where he set out to explore a new paradigm for cancer treatment in which living cells, rather than drugs, would work to fight the disease.

For more than a century researchers had studied the immune system as a way to fight cancer, and there had long been hope that cancer cells could be detected and killed by T cells. However, our immune systems evolved to fight pathogens invading from outside the body, not cancerous cells on the inside. Either our immune system doesn’t recognize cancer as a problem, or it attacks both cancer and healthy cells.

“Cancer spreads quickly because the body doesn’t see it,” Dr. June says. “When healthy cells mutate and become cancer
“We used an HIV virus as a Trojan horse to bypass the T cells’ immune system.”

CARL H. JUNE, MD

cells, to the system, they’re camouflaged and still look healthy. The immune cells never attack.”

To circumvent this issue, Dr. June and his team turned to genetic engineering and synthetic biology, using T cells, and B cells, which make antibodies that bind to kill bacteria. They realized they could insert the genes for B cell antibodies into T cells.

“We used an HIV virus as a Trojan horse to bypass the T cells’ immune system,” Dr. June says.

These T cells, genetically engineered to produce an artificial T cell receptor for use in immunotherapy, came to be called ‘chimeric antigen receptors’—thus, “CAR T cells”.

“Normally, T cells simply kill cells, but do not make antibodies,” Dr. June says.

“We take some of the body’s T cells and genetically retrain them to find a specific part of the biological code—the cancer fingerprint. Now we have antibodies within the T cells, and when they’re injected into a person with cancer, those CAR T cells hunt down and destroy all cells with that fingerprint. They divide and multiply by the millions and kill the tumor.”

All of this means CAR T cells are the first living drug in medicine, and for years they stay alive acting as a vaccine in the body.

In 2010, five-year-old Emily Whitehead was diagnosed with acute lymphoblastic leukemia, a disease that is usually cured. But after intensive chemo regiments Emily relapsed twice, her condition becoming even too grave for a bone marrow transplant, seemingly the only remaining option.

In a sequence of dramatic events worthy of a Hollywood script, Dr. June and his colleagues saw Emily go from the verge of multi-organ system failure to waking up on her seventh birthday with her cancer in deep remission. Suddenly, Dr. June found himself the face of what was being called a revolution in medicine.

In 2017, Dr. June’s breakthrough idea of using the HIV virus to deliver altered DNA to T cells led to the first FDA-approved personalized cell therapy for cancer. Today, there are two CAR T cell therapy products in use, one for acute lymphoblastic leukemia and one for diffuse large B-cell lymphoma.

Further, the principles behind Dr. June’s CAR T cell work could be used to design cell therapies targeted to treat other conditions such as autoimmunity, inflammation, degeneration, wound healing, and fibrosis.

THE HARRINGTON PRIZE FOR INNOVATION IN MEDICINE, established in 2014 by Harrington Discovery Institute and the American Society for Clinical Investigation (ASCI), honors a physician-scientist who has moved science forward with achievements notable for innovation, creativity and potential for clinical application.

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

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

HARRINGTON SCHOLAR-INNOVATOR AWARD
Supports physician-scientists whose research has the potential to change the standard of care in medicine. Each year, the Harrington Discovery Institute’s Scientific Advisory Board reviews applications from outstanding physician-scientists and selects those whose discoveries embody innovation, creativity and potential for clinical impact. ELIGIBILITY: MD OR MD/PHD; US AND CANADA.

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. ELIGIBILITY: MD OR PHD; US, CANADA AND UK.

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. ELIGIBILITY: MD OR PHD; US AND CANADA.

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. ELIGIBILITY: MD OR PHD; US.

NEW PROGRAMS

HARRINGTON-MSTP SCHOLAR AWARD AT CASE WESTERN RESERVE UNIVERSITY
In partnership with Case Western Reserve University (CWRU)
Supports Medical Scientist Training Program students whose research shows innovation and creativity, and the potential for progressing from scientific discovery to a medical therapy. ELIGIBILITY: MSTP STUDENTS AT CWRU.

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. ELIGIBILITY: MD OR PHD; UK.

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. ELIGIBILITY: MD OR PHD; US, CANADA AND UK.

Scholars in these new programs will be highlighted in the 2020-2021 Annual Publication.
CONGRATULATIONS 2020 SCHOLARS

2020 HARRINGTON SCHOLAR-INNOVATORS

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<tr>
<th>Name</th>
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<tbody>
<tr>
<td>RIZWAN HAQ, MD, PhD</td>
<td>Dana-Farber Cancer Institute</td>
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<td>KYU RHEE, MD, PhD</td>
<td>Weill Cornell Medicine</td>
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<td>DONALD WEAVER, MD, PhD, FRCP(C)</td>
<td>University Health Network</td>
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<td>MICHAEL HOLTZMAN, MD</td>
<td>Washington University</td>
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<td>STEPHEN STRITTMATTER, MD, PhD</td>
<td>Yale University</td>
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<td>TIMOTHY YU, MD, PhD</td>
<td>Boston Children’s Hospital</td>
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2020 HARRINGTON-MSTP SCHOLAR

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<td>YI FAN CHEN</td>
<td>Case Western Reserve University</td>
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2020 HARRINGTON SCHOLARS FOR CORONAVIRUS

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<th>Name</th>
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<tr>
<td>MICHAEL BARRY, PhD</td>
<td>Mayo Clinic</td>
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<td>ANASTASIA KHVOROVA, PhD</td>
<td>University of Massachusetts Medical School</td>
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<td>JAMES REYNOLDS, PhD</td>
<td>Case Western Reserve University/University Hospitals</td>
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<td>KATHERINE FITZGERAL, PhD</td>
<td>University of Massachusetts Medical School</td>
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<td>YULIA KOMAROVA, PhD</td>
<td>University of Illinois</td>
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<td>JOSEPH VINETZ, MD</td>
<td>Yale University</td>
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<td>BENJAMIN GASTON, MD</td>
<td>Indiana University</td>
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<td>ANNE MOSCONA, MD</td>
<td>Columbia University</td>
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<td>JAMES WELLS, PhD</td>
<td>University of California, San Francisco</td>
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<td>JEFFREY GLENN, MD, PhD</td>
<td>Stanford University</td>
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<td>MICHEL NUSSENZWEIG, MD, PhD</td>
<td>The Rockefeller University</td>
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<td>JAMES WILSON, MD, PhD</td>
<td>University of Pennsylvania</td>
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2020 HARRINGTON UK RARE DISEASE SCHOLARS

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<thead>
<tr>
<th>Name</th>
<th>Institution</th>
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<tr>
<td>PIETRO FRATTA, MD, PhD</td>
<td>University College London</td>
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<td>HELEN WALLER-EVANS, DPhil</td>
<td>Cardiff University</td>
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<td>HAIYAN ZHOU, MD, PhD</td>
<td>University College London</td>
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<td>ANGELA RUSSELL, DPhil</td>
<td>University of Oxford</td>
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<td>WYATT YUE, PhD</td>
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MEET OUR 2018 AND 2019 HARRINGTON SCHOLARS

To watch videos from some of our scholars, scan QR code with a smartphone camera
The work of Dr. Anderson’s lab could result in four breakthroughs for human health, all of which may come from a plant or a honeycomb.

The compounds at the center of this work are very long chain saturated (VLC-SFA) and polyunsaturated (VLC-PUFA) fatty acids, which are only found in retinal tissues, skin, brain, and sperm. A mutation in the gene that encodes the protein that makes these fatty acids causes Stargardt-like macular dystrophy, which affects children, eventually leading to blindness; while a different mutation causes spinocerebellar ataxia-34 (SCA34), a neurodegenerative disease that causes loss of balance in older persons. In addition, male infertility and dry skin often appear to be related to a loss or reduction of these fatty acids.

The saturated fatty acids can be obtained from beeswax and may be useful for treating SCA34 and skin diseases, but the polyunsaturated fatty acids must be chemically synthesized, though that process would not be economically feasible in poorer areas of the world.

“It’s never had a team like Harrington that wanted me to succeed, and was always there to help...from the financial aspects to the marketing aspects, to simply providing input.”

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

2019 HARRINGTON SCHOLAR-INNOVATOR

ROBERT E. ANDERSON, MD, PhD
George Lynn Cross Research Professor
Dean McGee Professor of Ophthalmology
Adjunct Professor of Geriatric Medicine
The University of Oklahoma

HOPE AT THE INTERFACE OF
BIOPHYSICS AND NATURE

FOCUS: Developing a way to make very long chain fatty acids as therapies to treat macular degenerative diseases, male infertility, gait problems, and dry skin.

“I’ve never had a team like Harrington that wanted me to succeed, and was always there to help...from the financial aspects to the marketing aspects, to simply providing input.”

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

2019 HARRINGTON SCHOLAR-INNOVATOR
Regulatory T cells (Tregs) are key regulators of the immune response, and defects in their numbers or function are tied to several autoimmune diseases. Dr. Bacchetta and her team are developing a novel method wherein a patient’s T cells turn into functional Tregs by gene addition, which could become a landmark approach to controlling many immune-mediated diseases. To prove this concept, their work is focused on a Treg cell therapeutic for IPEX syndrome, a rare disease inherited in males.

IPEX manifestations include severe diarrhea, eczema, enlargement of lymph nodes, and type 1 diabetes. Untreated, the disease is usually fatal during the first year of life. Bone marrow transplantation can be curative but is not always available; pharmacological immune suppression can prolong life and decrease some symptoms, but current treatments usually have unsatisfactory outcomes.

IPEX is caused by mutations of FOXP3, a key gene involved in immune regulation. IPEX patients’ Tregs cannot properly control the immune system responses and lose the ability to distinguish what is or is not worth fighting for to maintain health.

“The idea is to provide the functional Tregs IPEX patients are missing by inserting a normal FOXP3 gene into their T cells, then infusing them back into the patient,” Dr. Bacchetta says. “This work will also provide data which could broaden this Treg cell therapy to more common immune-mediated diseases, where patients have Treg cell defects not caused by FOXP3 mutations.”

“Outfoxing Mutated Genes

Focus: Genetically modified T cells to treat autoimmune disorders.

“Out our Harrington team has provided crucial support, such as helping us complete the preclinical work and providing precious regulatory and strategic advice to define the clinical protocol.”

Rosa Bacchetta, MD
Associate Professor of Pediatrics (Stem Cell Transplantation)
Stanford University
Mitochondria generate the majority of a cell’s energy and are vital to survival. Yet, maintaining a healthy mitochondrial population is challenging in peripheral nerves, which can be up to three feet in length (e.g., the sciatic nerves in our legs), requiring mitochondria to be actively transported from the spine to the nerve endings in our feet.

Mitochondria have genomes that are exchanged through mitochondrial fusion, which is mediated by proteins called mitofusins. “Mitochondria are mobile and can divide or fuse forming a more continuous network,” Dr. Dorn says. “The job of mitofusins is to pull the mitochondria close together in a very synchronized process.”

Genetic mutations of one mitofusin protein, mitofusin 2, cause a neurodegenerative condition called Charcot-Marie-Tooth disease, type 2A (CMT2A). There is no disease-altering therapy for CMT2A, which affects around 23,000 people in US,
typically in late childhood, with degeneration of nerves that leads to muscle atrophy in the arms and legs.

“With CMT2A, mutant mitofusins are inactive,” Dr. Dorn says. “Based on an intuitive understanding of what was happening with protein conformation, we were able to develop a compound that triggers mitofusin activation, evoking striking improvement in mitochondrial shape, fitness, and motility in CMT2A patient neurons and rescuing neuromuscular degeneration in a CMT2A mouse.”

With help from the Harrington Discovery Institute, Dr. Dorn hopes to provide those afflicted with CMT2A with far more effective medical management than physical therapy, walkers, braces and wheelchairs.

“With assistance from our Harrington Discovery Institute development team we now have a compound that looks like a drug.”
White blood cells continuously circulate through our bloodstream, ready to receive a signal that there is inflammation from an infectious disease or foreign invader. As they approach the pertinent location, they are temporarily trapped by adhesion molecules. The white blood cells then leave the blood vessel and migrate into the tissue to deal with the problem.

The signals calling for the making of adhesion molecules are sent by reelin, a glycoprotein made by the liver. By regulating the amount of adhesion molecules, reelin establishes the conditions that allow the immune cells to listen for inflammatory signals and respond appropriately.

In chronic inflammatory diseases, inflammation is caused by an overreaction of the body’s autoimmune response. “In most people, the responsiveness of their immune system is balanced so that the system only responds when tissue is damaged,” Dr. Herz says. “But in some people, the response is exaggerated, and a disease condition results from immune cells attacking the body’s own cells.”

“We have found that if we inject an antibody to neutralize reelin in the bloodstream, the inflammation alert level is reduced and we mitigate the autoimmune response,” Dr. Herz says. “We hope to develop such an antibody for therapeutic deployment in atherosclerosis, multiple sclerosis, rheumatoid arthritis, Crohn’s disease, and other disease conditions.”

“*Our Harrington team has helped us de-risk our strategy, which is crucial for the successful commercialization of any therapy.*”
AN UNCOMMON APPROACH TO AN EXTRAORDINARILY COMMON DISEASE

FOCUS: To develop a new class of safe and effective drugs to combat NAFLD.

In the US, heart disease, prostate cancer and high blood pressure are among the most commonly discussed health conditions, all considered particularly dangerous due to their lack of symptoms.

But a far less familiar, yet significantly more common symptomless condition is non-alcoholic fatty liver disease (NAFLD), which affects a quarter of the world’s population.

With NAFLD, too much fat is stored in liver cells, preventing the liver from functioning normally. It can lead to hypertension, cardiovascular disease, diabetes, even liver failure.

Dr. Hruz has made exciting headway on NAFLD with science that builds on the shoulders of insights gained through HIV research, as well as decades of glucose transporter biology studies. Glucose, essential for cellular respiration, crosses the membrane and enters cells via glucose transporters—proteins abbreviated as GLUT.

“In the liver, GLUT8 senses whether or not the body has enough fuel,” Dr. Hruz says.

“We are developing a new drug aimed at blocking this previously unrecognized mechanism—in essence tricking the liver into thinking it’s starving, which leads to increased burning of fat in order to provide more energy.”

Dr. Hruz’ team is working with the Harrington Discovery Institute to make the compounds more potent, and to ensure they work on GLUT8 and none of the other 13 human GLUTs.

“IT’S INDISPENSABLE TO HAVE Programs like Harrington’s—BECAUSE TO SUCCEED requires a whole different skill set than the scientific lab work. WE can’t do it alone.”

FOR MORE INFORMATION, PLEASE VISIT: harringtondiscovery.org/Videos
Myeloproliferative neoplasms (MPNs) are a group of diseases (polycythemia vera, essential thrombocythemia, primary myelofibrosis) in which excessive production of blood cells increases the risk of blood clots, often leading to strokes and heart attacks. Most commonly diagnosed after age 50, there are no curative therapies for MPNs, with many patients experiencing drug resistance and significant side effects. In some cases, patients' conditions can turn into acute leukemia.

For years Dr. Ji had been studying a relatively unknown protein called PLEK2, which is important for red blood cell development. Through this work he discovered that PLEK2 is regulated by JAK2 protein, which is often mutated in MPN patients. This mutation makes blood cells hyper-proliferate, causing disease.

“We had been working on the pathogenesis of MPN, focused on JAK2, and we discovered that JAK2 controls the expression of PLEK2,” Dr. Ji says. “When we knocked out PLEK2 in mouse models, we were thrilled to find that the result was a dramatically lower blood cell count and less blood clotting. We then performed high throughput screening and identified small molecule compounds that bind to PLEK2 and make it non-functional.”

With help from the Harrington Discovery Institute, Dr. Ji’s lab is working on optimizing the compounds—making them more potent, and testing pharmacokinetic data to see how the compounds are processed in the body. The goal is to use these compounds to treat MPN patients who have increased risks of blood clotting.

“*The Harrington consultants have been a tremendous help—their consultation is making a significant difference in the development of these compounds.*”

PENG JI, MD, PhD
Associate Professor of Pathology
Northwestern University Feinberg School of Medicine
Fuchs’ endothelial corneal dystrophy (FECD) is an age-related degenerative disorder in which the inner layer of the cornea degenerates, leading to corneal swelling, scarring, and loss of vision. In the United States, FECD affects one in 25 individuals over age 40 and is the leading indication for corneal transplantation, a procedure with post-op challenges and potentially serious complications.

In 2005, Dr. Mootha was recruited to the University of Texas Southwestern to implement new corneal transplant procedures for FECD. After years of performing corneal transplants, he felt that in the long run he could help more patients by studying the genetic basis of the disease.

Work done by Dr. Mootha’s lab and others has implicated toxic accumulation of expanded repeat RNA in the TCF4 gene as the molecular genetic basis of FECD. “We have developed small molecules called oligonucleotides that block the critical mutant repeat RNA that causes this disease, and in turn reverse the accumulation of this toxic RNA,” Dr. Mootha says.

“With the help of our Harrington team, we aim to further optimize our lead compound, develop formulations for safe and effective delivery, and identify biomarkers to facilitate human clinical trials,” he says. “If all goes well, we will have a therapy for FECD that’s as simple as a topical application or local injection administered in the clinic.”

In addition, Dr. Mootha’s work may hasten understanding of over twenty devastating neurodegenerative disorders caused by DNA repeat expansions.

“Our Harrington advisors bring vast scientific and industry knowledge to the table.”
Trypanosomatids are parasites that cause Chagas disease, leishmaniasis and human African trypanosomiasis, serious diseases afflicting millions of patients worldwide. Available treatments have many side effects, and because they are over five decades old, parasites have built up resistance, limiting their effectiveness.

Dr. Wetzel and her team have identified a small molecule that kills trypanosomatids in vitro as effectively as clinically-available drugs—a discovery that had some serendipity to it. “We were in the process of looking for compounds that affected how the parasites got into human immune cells,” Dr. Wetzel says. “Instead, by sheer accident, we found something that killed them.”

Her team found that if a compound were to interfere with tubulin, a protein crucial to the formation of the skeletal system in a one-celled parasite, the integrity of the cell structure would be compromised. “All cells have an internal skeleton that holds its shape, and is necessary for the cell to divide,” Dr. Wetzel says. “In a protozoan one-celled parasite, targeting tubulin locks its skeleton in place, preventing it from dividing, and within a few days, the parasite dies.”

With help from the Harrington Discovery Institute, Dr. Wetzel hopes to develop an important breakthrough in what is an extremely limited research and development pipeline for neglected tropical diseases.

“The Harrington Discovery Institute has helped us strategize how to get financing for a drug for a tropical disease that rarely occurs in the US.”
A SHORTCUT IN THE FIGHT AGAINST CANCER

FOCUS: Augmenting universal immunity to combat cancer.

In CAR T-cell therapy, a sample of a patient’s T-cells (part of the immune system) are modified, then reinfused into the patient where they kill the tumor cells expressing the specific antigens.

However, properly modifying the T-cells requires accurate characterization of the specific antigens, a difficult and lengthy process. Further, even when the T-cells recognize the cancer cells, the response might not be strong enough to destroy the cancer. Dr. Wu and his team appear to have found a way to enhance the immune system so that cancer cells die regardless of the type of antigens expressed by the tumor.

Dendritic cells are cells whose main function is to process and present tumor antigens to the T cells, but the body only sends a small amount of dendritic cells to a tumor. “We’ve linked albumin, a protein in blood, to Flt3L, a protein that helps produce dendritic cells,” Dr. Wu says. “The result is a molecule that tends to be delivered to the tumor location or lymph node, which in turn creates large amounts of dendritic cells, leading to many more T-cells capable of killing the cancer cells.”

For some cancers, this breakthrough platform of immunotherapy would render irrelevant the need to know what types of antigen are present in the tumor, and could be used in concert with chemotherapy and PD-1 inhibitors (drugs that activate the immune system to attack some tumors).

“Harrington has been amazing—they are true experts at helping you move from the very preclinical discovery phase to clinical trial.”

T.C. WU, MD, PhD
Professor of Pathology, Oncology and Molecular Microbiology & Immunology
The Johns Hopkins School of Medicine

FOR MORE INFORMATION, PLEASE VISIT: harringtondiscovery.org/Videos
Malaria is a major global health issue, a disease particularly dangerous to pregnant women and young children, causing over 200 million clinical episodes and 500,000 deaths annually.

“Parasites have developed resistance to all frontline antimalarial drugs,” Dr. Yeh says. “If we wait until resistance to antimalarial drugs has spread more widely before developing effective compounds, countless more people will be afflicted. Another critical factor is that development of therapeutics for the developing world is hampered by a relative lack of commercial pharmaceutical incentive.”

A promising drug target that has been proven in mouse malaria models is the enzyme PfFPPS/GGPPS, which has an important function in parasite metabolism. “Parasites are a single cell, and we have found that inhibiting PfFPPS/GGPPS removes a basic building block of the cell, so that it can’t survive,” Dr. Yeh says. “Once we block this enzyme, the cell can’t grow, can’t make new parasites, and it dies.”

PfFPPS/GGPPS as a target is not new, but compared to previous compounds, Dr. Yeh and her lab have developed one that is able to specify between a malaria enzyme and a human enzyme, as well as having improved drug qualities. In addition, their compound could be taken orally, a vastly simpler and faster treatment regimen than what currently exists.

By studying plasmodium biology, Dr. Yeh’s work offers the potential to have an important global health impact, as well as improving the economic incentives for drug development.

ELLEN YEH, MD, PhD
Associate Professor of Biochemistry, Pathology and Microbiology & Immunology
Stanford University

“For more information, please visit: harringtondiscovery.org/Videos”
PUTTING THE BRAKES ON ALZHEIMER’S


Alzheimer’s disease (AD), the most common form of dementia, is a brain degeneration causing disruptions in memory, cognition, personality, and other functions that eventually lead to death from brain failure. More than 5.8 million Americans now have AD, with approximately 500,000 new cases diagnosed each year. There is no cure for AD, nor can its progression be reversed.

In AD, amyloid plaques, neurofibrillary tangles and sustained pro-inflammatory cytokine signaling accumulate over time, causing dysfunction and neuronal death.

A drug able to halt or significantly slow disease progression at the pre-dementia stage, when only mild cognitive impairment is evident, would be a dramatic breakthrough.

There is growing evidence that increasing neuroprotection and reducing neuroinflammation will significantly delay AD onset and reduce its progression.

“We believe that neurosteroids (internal steroids synthesized within the brain) could work to delay AD onset and reduce progression,” Dr. Hodgetts says. “We have identified a compound that increases the levels of neurosteroids, lowers levels of pro-inflammatory cytokines and has good drug-like properties for a central nervous system drug.”

With support from his Harrington Discovery Institute advisory team, Dr. Hodgetts is working to improve the chemistry to achieve desired levels of potency and safety.

“The Harrington team has been very helpful, as academic labs do things differently from the industry drug discovery process.”
Approximately 44 million people worldwide live with Alzheimer’s disease (AD) or a related form of dementia, yet there are no effective treatments. It is believed that AD is caused by the accumulation of two proteins in the brain, amyloid beta and pTau.

“Much focus has been on preventing the buildup of amyloid beta and pTau,” Dr. Trushina says. “Yet in the brains of people with AD, neuronal dysfunction appears long before amyloid and pTau become problematic, and even before cognitive symptoms become evident. Neurons in the brain are critically dependent on mitochondria-produced energy; problems with energy homeostasis lead to neuronal dysfunction early in AD.”

Dr. Trushina and her team have developed a small molecule therapeutic targeted at mitochondria in order to improve energy production and utilization in neurons. “Scientists have traditionally avoided approaches involving mitochondria,” Dr. Trushina says. “The metabolic system is so complex, the concern has always been that anything affecting it could have unpredictable consequences.”

Dr. Trushina’s lab has developed compounds that, in mouse models of AD, improve glucose uptake and utilization, dendritic spine maturation, long-term potentiation, synaptic activity, cognitive function, and reduce amyloid deposition and pTau accumulation, oxidative stress and inflammation, ultimately blocking neurodegeneration.

In collaboration with the Harrington Discovery Institute, Dr. Trushina hopes to identify safe and efficacious preclinical and development small molecule candidates suitable for a Phase I clinical trial.
Retinitis pigmentosa (RP) is a group of inherited retinal disorders that lead to degeneration of photoreceptors (rods and cones) and blindness. With the exception of a costly gene replacement therapy for a subtype of Leber congenital amaurosis, there is no approved therapy for RP.

For decades, Dr. Martin has worked at the interface between chemistry and biology—making molecules and finding those having biological activity. In 2011, he sent a set of compounds to the Psychoactive Drug Screening Program at the University of North Carolina with the goal of identifying ones that selectively interact with receptors in the central nervous system. “I didn’t know what I was looking for...I just wanted to find something different,” he says.

“We were fortunate to find compounds that bound to the sigma 2 receptor, an enigmatic protein we helped identify as TMEM97,” Dr. Martin says. Although TMEM97 had never been associated with any degenerative retinal condition, he discovered TMEM97-binding compounds that protect rods and cones in an RP model. “This led us to believe that modulating this receptor would be a unique, gene-independent approach to treat any form of RP.”

With help from the Harrington Discovery Institute, Dr. Martin and his collaborators seek to develop a drug for RP that acts by a completely new mechanism of action and may be eventually applied to other retinal degenerative diseases.

“The consultants Harrington has provided have led us to think of new, potentially better molecules.”
FOCUS: Developing drugs to prevent or delay the onset and progression of Huntington’s disease and other DNA repeat expansion disorders.

When possible symptoms of Huntington’s disease (HD) appear, a blood test can tell whether a person has inherited the mutant gene. But the prognosis of the disease is so dire that many prefer not to know at all.

HD is a fatal disease that causes certain nerve cells in the brain to waste away. Symptoms usually don't appear until middle age, and may include uncontrolled movements, clumsiness, and balance problems.

HD is caused by a DNA repeat expansion, wherein a segment of repetitive DNA expands within the huntingtin gene, causing disease. HD is one of dozens of progressive neurological diseases caused by DNA repeat expansions.

Nearly a decade ago, Dr. Grabczyk found that one form of a minor DNA mismatch repair protein called MLH3 is responsible for DNA repeat expansion. His discovery was met with skepticism—“For a while, a colleague of mine and I were the only two people who believed it!” Dr. Grabczyk says.

“With help from the Harrington Discovery Institute we aim to inactivate this minor form of the MLH3 protein with splice-switching drugs so that it no longer causes DNA repeats to expand, while perturbing the mismatch repair system as little as possible.”

Dr. Grabczyk is hopeful that slowing expansion of the disease-causing DNA repeat will slow or stop the progression of HD, helping patients live longer, more fulfilling lives.

ED GRABCZYK, PhD
Associate Professor of Genetics
LSU Health Sciences Center in New Orleans

“The Harrington Discovery Institute is amazing, exactly what the world needs.”
FLIPPING THE SWITCH ON
ACUTE MYELOID LEUKEMIA

FOCUS: Developing a novel therapy for treating refractory and terminal AML.

Acute myeloid leukemia (AML) relapsed from chemotherapy is a highly aggressive disease with a five-year survival rate of just 27%. Adoptive cell therapy, including chimeric antigen receptor (CAR)-expressing T cells, is successful for treating leukemia expressing CD19 protein—but this approach has not been extensively explored for AML. There is a dire unmet need to develop more effective approaches using CAR T cells to treat AML.

Dr. Hua and his team have generated novel CD13CART, which targets specific cell surface protein CD13 that is highly expressed in the leukemia cells from most AML patients. “In preclinical models, these CAR T cells killed AML cells,” Dr. Hua says. “Remarkably, the killing activity of these CAR T cells can be controlled by a nanobody-containing switch—the switch is like a guided missile and takes the CAR T cells straight to the tumor. The result we have found is that the CAR T cells can completely regress the established and advanced tumor.”

Working with the Harrington Discovery Institute, Dr. Hua will evaluate whether this CAR T system is able to kill AML cells to treat patient-derived leukemia. It is hoped that these studies pave the way for developing novel and effective immunotherapy to cure drug-resistant AML.

XIANXIN HUA, MD, PhD
Professor of Cancer Biology
University of Pennsylvania

“The Harrington Discovery Institute shows great vision in helping scientists translate their ideas into potential practice use.”
Amyotrophic lateral sclerosis (ALS) causes the death of neurons controlling voluntary muscles. The disease onset is usually around age 60 and is typically fatal within two to four years. No cure is known—the goal of treatment is to improve symptoms.

More than 40 diseases are caused by expansions of simple sequence repeats dispersed throughout the human genome. The most common cause of ALS, as well as of frontotemporal dementia (FTD), is the GGGGCC repeat expansion in C9ORF72, a gene that provides instructions for making a protein that is found in various tissues. This repeat expansion causes the buildup and clumping of proteins, which in ALS leads to death of nerve cells.

“The nerve cell has difficulty degrading these clumps, which disturb many of the normal functions of the cell, leading to cell death,” Dr. Ichida says. “We screened thousands of chemicals to target C9ORF72, and found that inhibiting the protein PIKFYVE lowers levels of these clumps in nerve cells.”

There are many forms of ALS and FTD, and historically, specific forms have been targeted individually,” Dr. Ichida says. “PIKFYVE, which has never been a therapeutic target tested for neurodegeneration, is unique because it could work on multiple forms of both diseases.”
Rett syndrome is a rare chromosomal disorder that occurs almost exclusively in girls, usually recognized at 6 to 18 months, when symptoms arise that include motor abnormalities, severe seizures, absent speech, and autism. Individuals typically live wheelchair-bound for 40 years or more and require full-time care. There is no disease-specific treatment or cure.

Rett is caused by mutations on the X chromosome, specifically on the MECP2 gene that is crucial for neuronal development. Females have two X chromosomes, but only one is expressed in any cell, and the other is inactive.

In Rett girls, every affected cell harbors a normal but dormant copy of MECP2 on the inactive X chromosome. Dr. Lee’s aim is to alleviate disease by reactivating that dormant chromosome to restore MECP2 protein to the brain.

“There’s a central molecule, Xist RNA, that orchestrates the X chromosome shutdown,” Dr. Lee says. “Then DNA methylation (a process that plays a crucial role in regulation of gene expression) cements that shutdown. After years of trial and error, I had an epiphany: because no single compound can reactivate the X chromosome sufficiently, why not combine two modalities in such a way that the whole is greater than the sum of the parts? So we used drugs to target both of them—lo and behold, we got reactivation.”

Dr. Lee claims that this approach can potentially be applied to other diseases caused by mutations on the X chromosome.

“The Harrington Therapeutic Development team has made a huge difference to our drug discovery efforts, bringing logistical support not typically found in academia.”
In the Harrington Discovery Institute, Dr. Marshall has found scientists and drug development experts well-suited to his pragmatic approach to his work.

“The great thing about Harrington is that they didn't need to know everything about how our drug work—it was enough that it showed clear potential to benefit children with Angelman syndrome,” Dr. Marshall says.

Angelman syndrome (AS) is a severe neurogenetic disorder that affects thousands of children each year, characterized by developmental and intellectual disability, seizures, balance difficulties and other problems.

Long-term potentiation (LTP) is a persistent strengthening of synapses based on recent patterns of activity, a phenomenon believed by many neuroscientists to underlie learning.

AS arises from flaws in a gene called Ube3A, which in the brain normally limits the amount of a protein called Arc. Left unchecked, Arc thwarts the neuron signaling which is critical for LTP.

Dr. Marshall’s group designed a novel cyclic-peptide drug called CN2097, which reinstates signaling and thereby LTP, restoring neural functions in mice impaired by AS.

“Receptors are key elements in the communication of neurons, and by studying them we hope to understand at the molecular level how the brain functions,” Dr. Marshall says. “So, as often happens in science, the progress we’re making with a rare disease could lead to novel approaches for common illnesses—in this case, depression—a condition afflicting more than a quarter of a billion people worldwide.”

To learn more about how rare disease helps common disease, see page 17.

JOHN MARSHALL, PhD
Professor of Medical Science
Brown University

“Harrington funding allowed us to gather the data proving that our drug could get past the blood-brain-barrier.”
Huntington’s disease (HD) is a rare, inherited and fatal neurodegenerative disease with no treatment available. Symptoms usually appear between ages 30 and 50, and worsen over the next 10 to 25 years, ultimately leading to pneumonia, heart failure or other complications. There is no therapy to slow or prevent disease progression.

Mitochondria are often referred to as “the powerhouse of the cell”, and disease can occur when they are unable to completely burn food and oxygen to generate energy. As evidence suggests that mitochondrial dysfunction plays a critical role in the pathogenesis of HD, Dr. Qi and her team began work predicated on the theory that enhancing mitochondrial activity could be a therapeutic option.

“We demonstrated that improving mitochondrial dynamics with peptides was helpful in stem cells and mouse models of Alzheimer’s, Parkinson’s and HD,” Dr. Qi says. “But peptides often face challenges during drug development, so we have sought small molecules able to increase mitochondrial function.”

Dr. Qi and her team screened over 50,000 compounds, including CHIR99021, which has a history of useful applications in clinical biology. Her work showed that CHIR99021 enhanced mitochondria membrane potential and respiratory activity, as well as cell viability in cultured cells and diseased animals. “There is reason to hope that CHIR99021 would reduce neuronal loss, behavioral deficits and lethality in HD patients,” Dr. Qi says.

With help from the Harrington Discovery Institute, Dr. Qi and her team are conducting medicinal chemistry modification in further search of molecules that could become a novel therapeutic for HD, and potentially a range of neurological disorders.

“Being from an academic environment, it would be very difficult to translate our discoveries to real industry applications without help from the Harrington Discovery Institute.”
In neurodegenerative diseases, normal nerve cells develop abnormal functions ultimately leading to cell death. For many of these diseases there can be an associated loss of motor function control that can ultimately be fatal. As people live longer, neurodegenerative diseases are imposing increasing health and financial burdens.

RNA granules, aggregations of proteins and RNAs, appear in a cell when it is under stress, and are disease-related. Dr. Scoles and his team discovered that a stress granule protein, Staufen-1, is overabundant in several human and mouse neurodegenerative disease models such as Alzheimer’s disease, spinocerebellar ataxia type 2, and amyotrophic lateral sclerosis (ALS). (In the fly where Staufen was discovered, mutations lead to lineage extinction. Such genes are often named after European royal families that became extinct—thus, “Staufen”.)

His team then applied their expertise in producing antisense oligonucleotides (ASOs) that lower gene expression. They had previously used the method to target the ATXN2 gene toward developing a therapy for spinocerebellar ataxia type 2 (SCA2).

“We believe that using ASOs that lower Staufen-1 levels could be an effective therapeutic for treating several rare neurodegenerative disorders characterized by RNA granules,” Dr. Scoles says.
Glucosylceramide-based glycosphingolipidoses, including Gaucher disease type 3, Fabry disease, Tay-Sachs, Sandhoff disease, and GM1 gangliosidosis, are rare, often fatal disorders that involve the central nervous system (CNS). The absence of therapeutics that distribute to the central nervous system has rendered these disorders unresponsive to treatment.

A small molecule that distributes into the CNS and inhibits the synthesis of glycosphingolipid, a part of the cell membrane, may be of therapeutic benefit to patients afflicted with these diseases.

Dr. Shayman developed eliglustat, the first stand-alone oral treatment for Gaucher disease type 1 now in worldwide use. However, the poor brain exposure of eliglustat renders it unsuitable for the treatment of CNS-based glycosphingolipidoses. To address this need, he and his team developed compounds with structures similar to eliglustat with the aim of finding a molecule able to cross into the brain and retain metabolic activity.

“In effect, we looked at the chemical properties of eliglustat, identified those that are unfavorable to penetrating the brain, and designed compounds around those,” Dr. Shayman says. “Also, some patients cannot properly metabolize eliglustat, so it is necessary to design our new compounds around that liability as well, and find a therapy that is not subject to metabolism through this route.”

The findings of Dr. Shayman’s team holds promising results in mouse models of Gaucher disease type 3, and with support from the Harrington Discovery Institute they hope to progress into clinical trials toward an eventual treatment for this class of diseases.
THE HARRINGTON ADVANTAGE
Every scientist in academia aspires to have the results of their research published in a scientific journal. Often such findings are of immeasurable value to the scientific community and may inspire future groundbreaking discoveries.

Yet what if the scientist’s discovery has the potential to be translated into a therapeutic that can treat, prevent, or even cure a disease? Academic laboratories can be very good at doing research, and most universities have a technology transfer office to help commercialize promising discoveries. However, few of these offices are able to provide all the resources needed to develop a drug. An academic institution’s hope is that a pharmaceutical company will show interest after reading the scientist’s paper in a respected publication.

At the outset of the Therapeutics Development team’s (TDT) relationship with the Scholar and their institution, it is made clear to the technology transfer office that the Harrington Discovery Institute is working solely for the benefit of the researcher and her or his institution—Harrington takes no intellectual property rights at any time.

“What we’ve learned over many projects is that the model is at its best when our advisors and the project manager are incorporated into the scientist’s team, as if we were right there with them at their institution,” says Dr. Diana Wetmore, Vice President of Therapeutics Development. “When the scientist sees us as part of their team, that’s when the synergy of all the individuals involved, and their respective expertise, has the most impact.”

As they become familiar with the TDT, Scholars soon grasp the level of world-class expertise and resources made available expressly for the benefit of their project. It is an enviable therapeutics team—other than the Harrington Discovery Institute, perhaps no institution is capable of deploying, as needed, nearly 30 industry experts of such stature. Each has played key roles in shepherding drugs to market in the pharma and biotech sectors.

Indeed, the Therapeutics Development team is at the core of the original vision of The Harrington Project: to provide unparalleled technical and commercial drug development expertise to help promising scientific discoveries bridge the valley of death and become cures to help humankind.

The Scholars supported through The Harrington Project understand biology, physiology, chemistry, pharmacodynamics and genetics—they’re less familiar with the specialization of drug development. Over the course of the Scholar’s term, the TDT supports them and their research with key elements of clinical and commercial development.

“Before long, when industry is looking for assets to license from academia, they’ll check first with Harrington to see if any of our most promising projects are available.”

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different therapeutic indication in order to give a drug a better chance to transition from the lab to commercial development."

In addition to the complex work involved in modifying and optimizing a potential therapy on the road to clinical trials, the TDT provides crucial business development support for each project. Previously the business development advisory support would begin close to the completion of a Scholar’s term, but over the last two years Dr. Wetmore has made it a priority right from the beginning.

“We want to ensure that from the very start our business experts are interacting with the Scholars and their technology transfer offices, so when the time is right to start a dedicated partnering campaign, all gears are greased and everything is ready to go,” Dr. Wetmore says. “At that point we can work with the respective institution to get a solid, smart business plan in place, execute on it, and get that asset partnered.”

“For some projects, the business guidance we provide is as important as the technology development,” says Troy Gobbett, Senior Project Manager. “For the sake of the Scholars and their work, it’s our job to understand what the market needs. We keep up to speed on the industry landscape, conduct market analyses, assemble compelling pitch decks, and provide other forms of support to ensure a project will have partnering opportunities.”

The quality of its projects and expertise of the TDT is establishing the Harrington Discovery Institute as one of the world’s foremost drug development pipelines. “Before long, when industry is looking for assets to license from academia, they’ll check first with Harrington to see if any of our most promising projects are available,” says Dr. Wetmore.

**Q and A**

**Partnering with Academia**

We spoke with Marisa Naughton from the UT Southwestern Medical Center, a global leader in translating scientific discoveries into innovations that improve patient outcomes.

**What are some of the challenges your team faces?**

Our Office for Technology Development receives more than 160 invention disclosures per year. The major challenge we face, and one might say this is a good problem to have, is that we lack the bandwidth to advance innovative discoveries at the speed with which we would like. However, we have recently streamlined our process to enable better and faster outcomes. This has already begun pay off through increased industry engagement, commercialization and licensing.

**What are the benefits of receiving an HDI grant award?**

From a commercial standpoint, the experience helps validate the project. We let potential industry partners know, ‘This is a Harrington Discovery Institute project.’ The project has benefitted from a team of advisors with specific knowledge of the science and extensive experience bringing drugs to market.

Investigators see first-hand all the many pieces that make up the drug development process. It is more complex and time-consuming than most investigators would imagine. The HDI grant supports them during the most crucial part of the process—before industry is interested.

**How would you measure the value of an HDI grant?**

I’m not sure how we could put a value on what we’ve been given with the HDI grant. How do you measure the value of expertise? We’ve had the HDI team re-direct a project as the result of their evaluation of the science and commercial prospects. HDI accelerates the process. With HDI-supported Investigators, we ask them, “Tell me when you’ve reached your next milestone,” instead of “Tell me if you reach a milestone.”

**Is there anything that has surprised you during this process?**

I really appreciated the in-person project kick-off meeting for our 2019 Scholar-Innovator. We had everyone around the table and that really helped build a foundation of trust between all of us. I was surprised by how well the HDI team understood the Investigator’s science and how prepared they were to jump in and provide feedback. What I found very refreshing was that they didn’t hesitate to say when they didn’t know something—‘I don’t have the answer to that, but I will pull in a team member who does.” From the start, the HDI team members showed a genuine commitment to the success of the project.
ASSEMBLING A VIRTUAL PHARMA TEAM TO FIGHT INFLUENZA

In January, 2018, Dr. Jeffrey Glenn of the Stanford University School of Medicine was named a Harrington Scholar-Innovator, in recognition of his work toward developing a broad spectrum single dose therapeutic to treat all strains of Influenza A virus.

THE CHALLENGE
The focus of Dr. Glenn’s project was to develop a therapeutic for Influenza A, which presents in a constantly changing wide range of strains and subtypes that cause disease ranging from seasonal flu to lethal pandemics. Further, while common antiviral drugs target something in the virus, the viruses can often quickly mutate and become resistant to drugs.

THE SCIENCE
Influenza is an RNA virus, meaning that it has RNA as its genetic material. Dr. Glenn and his team had begun to develop a new class of antiviral agents that target critical viral RNA secondary structures—primary structures of RNA that have folded themselves into complex configurations, which are important for the correct function of many RNA molecules.

Secondary structures are highly conserved, meaning their genetic sequences have remained relatively unchanged. Dr. Glenn’s work is predicated on the idea that if a drug was developed to target an essential RNA secondary structure, because such structures aren’t susceptible to much change, they may have limited ability to mutate and escape from the drug.

Dr. Glenn and his team eventually isolated a segment of secondary structure within the virus’ RNA genome which, if targeted by the right therapeutic, would destroy the virus’ ability to assemble itself.

Moreover, because the targeted segment is highly conserved in all known isolates of influenza examined—including bird flu, H1N1, the 1918 pandemic—the proposed therapeutic would be a universal anti-flu drug capable of thwarting any current or future strains, including those resistant to current drugs on the market.

HARRINGTON EXPERTISE APPLIED
When HDI began working with the Glenn Lab, the task was to guide the science toward the creation of a safe, effective, single dose anti-viral therapeutic. As with all Harrington Scholars, a team of Strategic Advisors and Project Manager was assigned to the project.

Dr. Glenn’s therapeutic molecule of choice was an antisense oligonucleotide (ASO), a human-made nucleic acid that binds to RNA sequences and can prevent the expression of genes. Strategic Advisor Dr. Siew Ho was an ideal choice for the project’s scientific lead, with nearly 30 years’ experience in nucleic acids research and drug discovery.

Through regular meetings, Dr. Ho provided input on the data Dr. Glenn’s team generated and on the experiments they were designing. Part of her role as an advisor was to anticipate any potential hurdles, helping the scientist and their team chart out a clear path to the clinic.

DR. GLENN’S CORE HDI PHARMA TEAM

SIEW PENG HO, PhD
Scientific Lead

JAN ROSENBAUM, PhD
Business Development Lead

TROY GOBBIETT, MS, PMP
Sr. Project Manager
Dr. Ho shared insights, such as how to improve upon the therapeutic candidates, and which of the various antisense mechanisms were likely to yield more potent molecules. At times she would bring to the attention of Dr. Glenn’s team potential toxicities of some of the delivery agents used, and/or whether they’d been approved for clinical use.

During the development of a drug, it is crucial that the investigator be thinking about the path to market. Enter Strategic Advisor Dr. Rosenbaum, a drug development professional with more than 25 years of pharma and biotech management expertise in the development of small molecule, peptide, and protein therapeutics. “Jan helped us think in terms of who our clinical trial population is going to be, and what studies need to be in place to move into clinic,” Dr. Glenn said.

At one point, both Dr. Rosenbaum and Dr. Ho felt that the FDA was going to push back on the formulation, as it was toxic above a certain concentration, which would limit the dosage. “Jan and Siew knew that those studies were cancer-related, which is different from other indications,” Dr. Glenn said. “Respiratory indications, like ours, have an even higher hurdle because the lungs irritate so easily.”

Dr. Glenn’s therapeutic was to be administered through inhalation, so the advisors found an organization skilled at developing inhalation formulations, and studies were then designed around the new delivery direction.

As Project Manager, Mr. Troy Gobbett ensured the Advisors and the academic institution’s teams met monthly, at times more often, to look at the latest data and progress made in the lab. Keeping all parties in the loop, he informed the teams on what studies were due to occur, acting as a conduit between entities and ensuring all contracts were in place, and that there was consensus on the protocols of each study, to name just a few of his responsibilities. Mr. Gobbett has a Master of Science in Molecular and Developmental Biology, and has held leadership positions at major pharmaceutical firms.

RESULTS

When Dr. Glenn became a Harrington Scholar, his team was in the process of screening compounds to pinpoint the most effective and safe way of targeting RNA secondary structures. By the end of the two-year term, HDI had helped progress the work to lead optimization, wherein the chemical structure of the lead compound can now be advanced to the clinic.

“If successful, this therapeutic will significantly boost our ability to ward off pandemics, while dramatically reshaping the landscape of antiviral drug development—allowing us to be proactive, rather than reactive, to emerging viral threats. Indeed, we can leverage the lessons learned in our project and now apply the same approach to virtually any virus of interest.”

JEFFREY GLENN, MD, PHD
After working on a project with a Harrington Scholar, the Therapeutic Development team (TDT) may determine that the project is promising and would benefit from additional funding beyond the initial grant. When this occurs, the project comes before the Investment Advisory Board (IAB), which will pose questions to the Scholar’s Advisors such as:

• Why would this therapy be an improvement over existing treatment options?

• Why has no one solved this before?

• Would the product offer better efficacy, improved delivery, faster recovery?

One question in particular underscores the remarkable dedication, not to mention patience, these investigators must have as they journey through the drug discovery and drug development process:

• What is the expected timeframe for the product to reach the market?

Note: In the US it takes an average of 12 years for an experimental drug to advance from the laboratory to the medicine cabinet.

That the Scholar’s work was presented to the IAB is a notable milestone, as it means that this technology has potential, and for the project to move forward, additional investment is required. Hence it is important that the IAB performs a neutral, objective analysis of the project’s value proposition, in terms of likely industry and investor interest, as well ensuring that HDI philanthropic funds are utilized where they have the greatest impact.

Each member of the IAB has decades of industry and/or venture funding experience, so the board is able to see every Scholar’s project from the industry investor commercialization perspective. They advise how the project, with help from the TDT, can best work toward objectives that would make it attractive to a biotech or pharmaceutical partner.

“What we bring to the table is a broader view of the market,” says Dr. John Rice, the IAB Chair. “Everyone on our team has been in leadership roles in the pharmaceutical industry or invested in and worked with startup companies with new technologies. They are each qualified to determine the commercial potential of a Scholar’s proposal, and whether we concur with the project’s timelines and objectives as they’ve been proposed.”

When the IAB meets, every member contributes with suggestions and concerns, and they keep at it until everyone reaches a consensus. “Often a project that is initially denied follow-on funding eventually gets it,” Dr. Rice says. “It may end up being for a different clinical indication, or an approach that the Scholar didn’t realize would make a large enough difference.”

“Whether we approve the funding or not, every bit of advice that we impart to the investigators improves their chance at getting drugs through the difficult and riskier early stages of funding, the so-called valley of death.”

MAXIMIZING IMPACT FROM PHILANTHROPIC FUNDS

JOHN RICE, PhD
Chair, Investment Advisory Board
Harrington Discovery Institute
Managing Director, CincyTech

FOR MORE INFORMATION, PLEASE VISIT: harringtondiscovery.org/IAB
A Harrington Scholar award creates far more value for the investigator than simply the benefits derived during the term of the award.

Not only do Harrington Scholars have the opportunity to access several rounds of capital, plus invaluable drug development and business development support from industry experts, they then have access to mission-aligned partners like BioMotiv, a biotech accelerator that oversees further development of the therapeutic product toward human testing and on to a deal with a larger partner.

Conceived as part of The Harrington Project, BioMotiv is a for-profit entity that is able to source projects from the Harrington Discovery Institute as well as from university and research institutions, disease foundations, and industry sources, allowing for a portfolio of diverse scientific discoveries to be advanced into therapeutics for patients.

BioMotiv also has an alliance with Bristol-Myers Squibb (BMS) and a longstanding strategic partnership with Charles River Laboratories, which enables BioMotiv to quickly advance programs and achieve economies of scale in drug development.

Prior to joining BioMotiv, Dr. Satish Jindal was a co-founder of several successful biotech companies, such as NeoGenesis (acquired by Schering Plough, now Merck), Verastem, Elicio, and others. Since coming on board as CEO, he has initiated a shift in the BioMotiv model. “Where historically we invested alone in single-asset companies, we now focus more on assets targeting multiple indications and platforms,” he says.

BioMotiv is now bringing in other investors more frequently. “When we are spinning out a company, we do it through syndication with other like-minded investors,” Dr. Jindal says. “It is a balancing act between investing in interesting early-stage, higher risk projects, and later stage projects where risk has been minimized, which of course appeals to investors.”

As always, HDI is a critical source for the BioMotiv pipeline. “We diligently keep our eye on projects being supported by HDI—if it looks like good transformational science, which also can be translated to a product opportunity in a timely fashion, then we’re very interested,” Dr. Jindal says.

Current BioMotiv HDI-related projects include:

- Koutif, a company launched by BioMotiv that is developing a novel therapeutic to treat Crohn’s disease, inflammatory bowel disease and other inflammatory conditions. At this writing, BioMotiv is helping Koutif in its work to improve efficacy and safety in the project’s parent molecule (the active form of the original molecule).

- OptiKira, formed by BioMotiv in 2015, which may soon enter clinic with a development candidate aimed at treating retinitis pigmentosa, idiopathic pulmonary fibrosis, cancer and amyotrophic lateral sclerosis.

- Allinaire Therapeutics’ disease-modifying approach to pulmonary arterial hypertension, which targets a unique mechanism with great transformation science behind it.

Dr. Jindal’s decision to head up BioMotiv is a testament to The Harrington Project model. “The Harrington Discovery Institute provides access to an unprecedented breadth of ideas which can transform development of new medicines,” he says. “HDI uses its philanthropic funding to mature those ideas to a stage where BioMotiv can help in further translating selected de-risked ideas into products that improve the standard of care.”
The Cleveland Foundation has a long history of funding initiatives aimed at mitigating, preventing or curing diseases affecting Northeast Ohio, the United States, and the world. From polio to AIDS to COVID-19, this venerable institution has used the power of philanthropy to make innovative, impactful and internationally-recognized contributions to improve the human condition.

In late 2018, the Cleveland Foundation saw the thrilling potential for medical breakthroughs that the Oxford-Harrington Rare Disease Centre (OHC) would bring to the global rare disease space and awarded the Harrington Discovery Institute a $1,000,000 grant in support of the OHC’s creation.

“When you look at how many people out there are suffering from a disease that lacks funding or research, the value of the work to be done by the OHC will be beyond measure,” says India Pierce Lee, Senior Vice President, Program at the Cleveland Foundation. “In 1983, Congress passed the Orphan Disease Act to incentivize the development of drugs to treat rare diseases. At that time there were about 5,000 known rare diseases—today there are more than 7,000, affecting over 300 million people worldwide, with about 200 new rare diseases discovered each year. This was a real eye-opener for us, and to support the OHC fits the sweet spot of the Cleveland Foundation."

“Two years ago, when we considered the lives that will be saved, and the suffering that will be prevented by therapies developed with help from the OHC, we were very excited when we put together this grant. We work in many arenas to raise money from donors for medical research, always looking for strong collaborative initiatives with the potential to provide long-term results,” Ms. Lee says. “For these two drug research giants to work together, it not only will bring hope and answers for those suffering from rare diseases, but it will also further establish Cleveland as a global center for groundbreaking research.”

For Ms. Lee, the potential to provide therapies for children who suffer from a rare disease is the most gratifying aspect of the grant. “The OHC will focus on three core scientific themes: rare cancers, developmental disorders, and neurological disorders. Within these rare disease areas are millions of children who won’t see their fifth birthday,” she says. “This grabs at our hearts—how there are no drugs available for so many of these diseases.”

“For the Cleveland Foundation, it only makes sense to help the Oxford-Harrington Rare Disease Centre be at the forefront of this, so that in, say, 20 years we can look back and see how many treatments have helped afflicted people around the world.”
There are more than 7,000 known rare diseases, and it’s probably safe to say that you haven’t heard of 99% of them. But more people than ever are aware of the presence of rare diseases within the human condition, and here in the United States that’s thanks largely to the efforts of NORD, the National Organization for Rare Disorders. For four decades NORD has served as the hub of the rare disease community, driving progress for rare disease patients and patient organizations.

In 2008, NORD created the first Rare Disease Day, to raise awareness and generate action on behalf of the more than 350 million people worldwide who have a rare disease. Rare Disease Day is now celebrated annually on the last day of February in over 100 US cities and close to 500 cities worldwide. In 2020, the Harrington Discovery Institute at University Hospitals hosted Ohio’s first Rare Disease Day Summit in Cleveland.

Patients, families, caregivers, medical professionals and industry representatives discussed the challenges rare disease patients face and how to make a difference in the lives of Ohio’s rare disease patients. Presentations addressed the challenges surrounding the diagnosis and treatment of rare diseases and the lack of approved treatment options. Guests included individuals representing the patient, pharma, and researcher/clinician perspectives.
Global leaders in science, medicine and academia convened in Cleveland, Ohio for the Seventh Annual Harrington Scientific Symposium to share knowledge and celebrate successes. Working together toward a common goal was a theme that ran throughout the event held May 22-23, 2019.

"We are unified by a shared problem, which is that there are over 10,000 medical diseases, and only 500 of them are treatable," said Jonathan S. Stamler, MD, President of Harrington Discovery Institute, during the Symposium’s Keynote Address.

Dr. Stamler provided an overview of the Institute’s programs, new initiatives and strategic partnerships that were developed to address the critical lack of cures.

Harrington Project founder Ronald G. Harrington reflected on the progress made in the Institute’s seven-year history, and encouraged the audience of scholars, advisors, team members and other stakeholders to redouble their efforts. "Let’s continue, and even ramp up, our incredibly hard and important work of accelerating discoveries into medicines that treat and cure disease," Mr. Harrington said.

David M. Gamm, MD, PhD, of University of Wisconsin-Madison and 2016 Gund-Harrington Scholar, gave the Scholar Experience presentation, sharing his experience working with the Therapeutics Development Team on his project aimed at advancing treatments for inherited retinal degenerative diseases. "This has been a long and winding road," Dr. Gamm said. "With the help of the team that we’ve had through the Harrington Discovery Institute it has really been a very fruitful and fun experience."

The Keynote Lecture was given by Carl H. June, MD, Richard W. Vague Professor in Immunotherapy in the Department of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania. Dr. June, the 2019 Harrington Prize recipient (see pages 20-21), presented some of his breakthrough work and inspired the audience with a story of a young cancer patient he and his team treated with a modified version of her own T-cells. The patient later went into remission. "It’s a cell therapy. It’s a new medicine. In my case, I’ve worked on it for 30 years and finally got it out clinically. It takes a long time," Dr. June said.

Morgan Stanley Global Impact Funding Trust (GIFT) president Melanie Schnoll Begun spoke on the second day of the Symposium about Morgan Stanley GIFT Cures (see page 9) the new partnership between Morgan Stanley and Harrington Discovery Institute. "Morgan Stanley GIFT Cures is enabling our clients to look at curated opportunities that have potential to make a real difference in the lives of millions who are impacted by the most difficult diseases," Ms. Schnoll Begun said.

Medical luminaries and members of Harrington’s advisory boards were in attendance including David Ginsburg, MD, William G. Kaelin, Jr., MD, Barbara Kahn, MD, Louis Kunkel, PhD, Beth Levine, MD (deceased), Charles Sawyer, MD, Andrew Schafer, MD, and Michael Welsh, MD.

Dr. Kaelin, who with two other physician-scientists won the 2019 Nobel Prize in Physiology or Medicine, gave a presentation over dinner, sharing inspirations and insights from his esteemed career.
HARRINGTON SCHOLARS 2013–2020

2020 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

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

2016 HARRINGTON SCHOLAR-INNOVATORS
NUNZIO BOTTINI, MD, PhD
*La Jolla Institute for Allergy and Immunology

STANLEY N. COHEN, MD
Stanford University

M. PETER MARINKOVICH, MD
Stanford University

2020 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 MOOTH, MD
UT Southwestern

DAWN M. WETZEL, MD, PhD
UT Southwestern

T.C. WU, MD, PhD
The 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

BHUVANESHWAR SINGH, MD, PhD
Memorial Sloan Kettering Cancer Center

DAVID B. SYKES, MD, PhD
Massachusetts General Hospital

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

2015 HARRINGTON SCHOLAR-INNOVATORS
ROBERT A. BONOMO, MD
Case Western Reserve University

JANAKI N. BURSTLE, MD
Mayo Clinic

VINAY K. CHAUHAN, MD, PhD
University of Missouri

2014 HARRINGTON SCHOLAR-INNOVATORS
NUNZIO BOTTINI, MD, PhD
*La Jolla Institute for Allergy and Immunology

STANLEY N. COHEN, MD
Stanford University

M. PETER MARINKOVICH, MD
Stanford University

2013 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 MOOTH, MD
UT Southwestern

DAWN M. WETZEL, MD, PhD
UT Southwestern

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

ELLEN YEH, MD, PhD
Stanford University

2012 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

BHUVANESHWAR SINGH, MD, PhD
Memorial Sloan Kettering Cancer Center

DAVID B. SYKES, MD, PhD
Massachusetts General Hospital

2011 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

2010 HARRINGTON SCHOLAR-INNOVATORS
ROBERT A. BONOMO, MD
Case Western Reserve University

JANAKI N. BURSTLE, MD
Mayo Clinic
GEOFFREY S. PIT, MD, PhD  
Duke University  

IRA A. TABAS, MD, PhD  
Columbia University  

2014 HARRINGTON SCHOLAR-INOVARATORS  

JAYAKRISHNA AMBATI, MD  
*University of Kentucky  

DARREN R. CARPIZO, MD, PhD  
Rutgers Cancer Institute of New Jersey  

GARRET A. FITZGERALD, MD  
University of Pennsylvania  

MARK S. HUMAYUN, MD, PhD  
University of Southern California  

JOHN N. KHEIR, MD  
Boston Children’s Hospital  

RAHUL M. KOHLI, MD, PhD  
University of Pennsylvania  

GAVRIL W. PASTERNAK, MD, PhD  
Memorial Sloan Kettering Cancer Center (In Memoriam)  

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-INOVARATORS  

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. LIEHTHKE, MD, PhD  
Duke University  

SANFORD D. MARKOWITZ, MD, PhD  
Case Western Reserve University  

SCOTT A. OAKES, MD  
University of California, San Francisco  

FEROZ R. PAPA, MD, PhD  
University of California, San Francisco  

JONATHAN D. POWELL, MD, PhD  
The Johns Hopkins University  

ROBERT B. WILSON, MD, PhD  
University of Pennsylvania  

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  

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 SCHOLAR  

TRAVIS L. DUNCKLEY, PhD  
Arizona 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  

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  

2016 GUND-HARRINGTON SCHOLAR  

THOMAS A. REH, PhD  
University of Washington  

2015 GUND-HARRINGTON SCHOLARS  

ALBERT R. LA SPADA, MD, PhD  
University of California, San Diego  

2016 OXFORD-HARRINGTON SCHOLAR  

VALENTINE MACAULAY, MD, PhD, FRCP  
University of Oxford  

2015 OXFORD-HARRINGTON SCHOLARS  

HELEN MCSHANE, MD, PhD, FRCP  
University of Oxford  

2014 OXFORD-HARRINGTON SCHOLAR  

CLAUDIA MONACO, MD, PhD, FESC  
University of Oxford  

2014 OXFORD-HARRINGTON SCHOLAR  

ALISON SIMMONS, MD, PhD  
University of Oxford  

TO LEARN MORE, PLEASE VISIT:  
harringtondiscovery.org/Scholars

*Scholar institution at time of award
To advance discoveries by physician-scientists, and all scientists in areas of unmet therapeutic need, into medicines for the benefit of society.