2012 – 2013
Celebrating a Year of ACCOMPLISHMENTS
Dear Friends and Colleagues,

In early 2012, University Hospitals and the Harrington Family Foundation established the Harrington Discovery Institute. This was the catalyst for an even larger vision and an ambitious goal: Develop a bold new model that aligns the structure and mission of for-profits and nonprofits to create an organized, dedicated system for drug development. By identifying promising scientific discoveries and linking the researchers responsible for them with scientific and business experts in drug development, we set out to build a bridge over the “Valley of Death” – the chasm between the laboratory and commercialization of new therapies.

Over the past year, we have laid a solid foundation for that bridge. We established a Scientific Advisory Board of internationally renowned physician-scientists. We identified Goutham Narla, MD, PhD, as the first resident Harrington Distinguished Scholar early career awardee and, through a competitive application process, awarded nearly $1 million in grants to our first class of 10 Harrington Discovery Institute Scholar-Innovators to accelerate their research. To provide the infrastructure to optimize drug development based on their work, we created the Innovation Support Center to provide expert guidance from highly experienced drug development professionals, mentoring and assistance with commercialization. Positioned at the other end of the bridge is another resource for the Harrington Scholar-Innovators, BioMotiv, a for-profit development company. Driven by University Hospitals’ research mission and the passion of the Harrington family and other visionary supporters to accelerate breakthrough discoveries into medicines, BioMotiv will advance a portfolio of the most promising products through human proof-of-concept studies.

Our Distinguished Scholar and the Harrington Scholar-Innovators, from some of the most-respected academic medical institutions in the country, share a laser-sharp focus on advancing scientific innovations that have the potential to conquer disease and relieve human suffering. The Harrington Discovery Institute will provide core resources and support needed to translate their knowledge and research into therapeutic breakthroughs that are commercially viable.

These accomplishments represent only the beginnings of a model that we believe will transform the drug development process. When fully scaled, the Harrington Discovery Institute plans to have the capacity to develop 40 technologies simultaneously every three years. It is an aggressive agenda that no other organization has attempted, and it promises to be a great adventure of discovery. I invite you to join us on our journey.

Sincerely,

Jonathan Stamler, MD
Director, Harrington Discovery Institute
TABLE OF CONTENTS

Harrington Discovery Institute Timeline .............................................. 5

History of the Physician-Scientist .................................................. 6

2012 Harrington Distinguished Scholar: Goutham Narla, MD, PhD ........ 8

About the Harrington Discovery Institute Scholar-Innovator Grant Program .... 10

Harrington Discovery Institute Scholar-Innovators

<table>
<thead>
<tr>
<th>Name</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marc I. Diamond, MD</td>
<td>12</td>
</tr>
<tr>
<td>Roger A. Greenberg, MD, PhD</td>
<td>14</td>
</tr>
<tr>
<td>Geoffrey C. Gurtner, MD, FACS</td>
<td>16</td>
</tr>
<tr>
<td>Richard N. Kitsis, MD</td>
<td>18</td>
</tr>
<tr>
<td>Wolfgang B. Liedtke, MD, PhD</td>
<td>20</td>
</tr>
<tr>
<td>Sanford D. Markowitz, MD, PhD</td>
<td>22</td>
</tr>
<tr>
<td>Scott A. Oakes, MD, and Feroz R. Papa, MD, PhD</td>
<td>24</td>
</tr>
<tr>
<td>Jonathan D. Powell, MD, PhD</td>
<td>26</td>
</tr>
<tr>
<td>Larry S. Schlesinger, MD</td>
<td>28</td>
</tr>
<tr>
<td>Robert B. Wilson, MD, PhD</td>
<td>30</td>
</tr>
</tbody>
</table>

Innovation Support Center ....................................................... 32

Harrington Discovery Institute Scientific Advisory Board .................... 34

BioMotiv ......................................................................................... 36

BioMotiv Advisory Board .............................................................. 37

Harrington Discovery Institute Scientific Symposium .......................... 38

The Harrington Family ..................................................................... 39
The Harrington Discovery Institute at University Hospitals Case Medical Center is part of the $250 million Harrington initiative, which includes philanthropic and institutional support and a mission-driven, for-profit bio-accelerator. The Harrington Discovery Institute was established early in 2012 for the express purpose of supporting physician-scientists by enabling them to transform their groundbreaking discoveries into breakthrough therapies and medicines that improve patients’ lives.

Here we present the significant milestones that the Harrington Discovery Institute has achieved in this historic first year.

Among the nation’s leading academic medical centers, University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a nationally recognized leader in medical research and education.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>February 2012</td>
<td>Harrington family makes $50 million gift to establish the Harrington Discovery Institute and launches The Harrington Project for Discovery &amp; Development.</td>
</tr>
<tr>
<td>May 2012</td>
<td>Harrington Discovery Institute Scholar-Innovator grant competition launched. Up to 10 grants will be made annually to provide financial support and professional mentoring to physician-scientists with breakthrough, patient-inspired clinical research projects.</td>
</tr>
<tr>
<td>June 2012</td>
<td>Harrington Distinguished Scholar Program launched. Goutham Narla, MD, PhD, named as first Harrington Distinguished Scholar (Early Career Award).</td>
</tr>
<tr>
<td>August 2012</td>
<td>Applications close for 2012 Harrington Scholar-Innovator grants. By the time the application period closes, 130 applications from distinguished physician-scientists at 53 prestigious institutions have been received.</td>
</tr>
<tr>
<td>December 2012</td>
<td>Harrington Scholar-Innovator inaugural class selected. These 10 Harrington Scholar-Innovators will be provided with two years of funding up to $200,000 and focused direction on the steps necessary to move their discoveries forward through early-stage research to possible clinical development.</td>
</tr>
<tr>
<td>January 2013</td>
<td>Innovation Support Center established. Perry B. Molinoff, MD, named Innovation Support Center director.</td>
</tr>
<tr>
<td>February/March 2013</td>
<td>Innovation Support Center Advisory Board selected.</td>
</tr>
<tr>
<td>April 2013</td>
<td>Harrington Discovery Institute and American Society for Clinical Investigation announce the Harrington Prize for Innovation in Medicine.</td>
</tr>
<tr>
<td>May 9 – 10, 2013</td>
<td>First Harrington Discovery Institute Scientific Symposium held in Cleveland.</td>
</tr>
</tbody>
</table>
Jenner, Lister, Salk. The names of physician-scientists who have left their mark on medical history are as familiar to today’s physicians as the Hippocratic Oath.

“Physician-scientists” can be defined as those with MD degrees (alone or combined with other advanced degrees) who devote a substantive percent of their professional effort to research anywhere along the entire spectrum of biomedical inquiry, according to Andrew I. Schafer, MD, Chairman of the Department of Medicine, Weill Cornell Medical College, New York. In his book, The Vanishing Physician-Scientist? and paper of the same name, published in Translational Research in 2010, Dr. Schafer describes the sweeping scope of research that is the physician-scientist’s domain.

Jonathan S. Stamler, MD, Director of the Harrington Discovery Institute at University Hospitals Case Medical Center, calls the nation’s 14,000 physician-scientists “the individuals who are best-suited to identify and drive discoveries into usable products for patients...These individuals are mission-oriented to pursue translating fundamental scientific knowledge into new therapies for their patients. The orientation of physician-scientists makes them uniquely capable of identifying solutions.”

Physician-scientists have always ranked among the most honored and most honorable of medical professionals, responsible as they are for numerous breakthrough discoveries that have helped to eradicate disease and alleviate human suffering. Says 2013 Harrington Discovery Institute Scholar-Innovator Marc I. Diamond, MD, in speaking of his father, Ivan Diamond, MD, PhD, noted researcher and founding director of the Ernest Gallo Clinic and Research Center at the University of California, San Francisco, “My father impressed upon me the excitement and joy of life as an academic physician, and the worthiness of the work.”

Yet today, the physician-scientist may be in danger of becoming a vanishing breed. A Yale University report in 2010 concluded that there are many barriers for today’s physician-scientist to overcome, citing the under-representation of physician-scientists on medical school admissions committees; a dearth of physician-scientists on bedside teaching rounds; and a disproportionate tendency for women to leave research at all stages of their careers. Add to that limited and constrained federal grantmaking, skyrocketing research costs and declining approval of new treatments, and the survival of the physician-scientist looks questionable.

The Harrington Discovery Institute is dedicated to helping physician-scientists not only survive but thrive. By sourcing the nation’s most promising physician-scientists and providing breakthrough discoveries with the financial and human capital in the form of expert industry guidance to advance projects from discovery through human proof-of-concept, the Harrington Discovery Institute will be a driving force to support our nation’s corps of physician-scientists and in the process benefit patients and society.

In the next pages, you are invited to meet the 2013 Harrington Scholar-Innovators who are carrying on the proud tradition of the physician-scientist.
UH Case Medical Center, as the primary affiliate of Case Western Reserve University School of Medicine, has a long tradition of encouraging the physician-scientist by creating a supportive environment and infrastructure that values their work. For nearly a century and a half, UH and Case Western Reserve University School of Medicine physician-scientists have been making groundbreaking discoveries that contribute to the transformation of medical care.

1915  David Marine, MD, proves iodine deficiency as the cause of goiter

1919  Two pediatricians at UH Rainbow Babies & Children’s Hospital develop and patent one of the first baby formulas

1923  Corneille Heymans, MD, visiting scientist in the Department of Physiology, receives the Nobel Prize in Medicine for his work on carotid sinus reflexes

1950s  Hymer Friedell, MD, PhD, pioneers the use of radioisotope therapy in treating malignancies

1954  Frederick C. Robbins, MD, shares the Nobel Prize in Medicine for his work on the polio virus, which laid the groundwork for the polio vaccine

1958  Benjamin Spock, MD, begins groundbreaking child-rearing research at UH Rainbow Babies & Children’s Hospital

1970s  Oscar Ratnoff, MD, discovers blood clotting factors to explain the waterfall sequence in blood clotting

1980  Neonatologists and respiratory therapists at UH Rainbow Babies & Children’s Hospital develop a high-frequency jet ventilator to more safely treat premature babies

1988  George H. Hitchings, MD, PhD, receives the Nobel Prize in Medicine for his contributions to developing drugs for leukemia, organ transplant rejection, gout, herpes virus infections and AIDS-related malaria and bacterial and pulmonary infections

1992  Nancy Oleinick, PhD, co-discovers Pc4, a drug used in photodynamic therapy to destroy cancer cells

1995  Sanford D. Markowitz, MD, PhD, discovers the RII genetic link for colon cancer

2000s  Mukesh K. Jain, MD, identifies a family of factors termed Kruppel-like factors that regulate critical aspects of cardiovascular biology, innate immunity and metabolism

2003  Scot Remick, MD, discovers a new thyroid cancer cure

2009  Daniel I. Simon, MD, identifies a novel biomarker called MRP-8/14 that predicts the risk of future heart attack and stroke
Goutham Narla, MD, PhD, was at a crossroads in his career.

He had the option of working in the pharmaceutical industry on drug development, a choice that would mean abandoning his own science in favor of working on a drug company’s projects. His other option was to pursue his own research by forming a company, but he knew that the process of moving his work from laboratory to patient care would be very challenging.

A chance dinner with a fellow research scientist – Mukesh K. Jain, MD, Director, Harrington Scholar Program for the Harrington Discovery Institute at University Hospitals Case Medical Center; Chief Research Officer and Ellery Sedgwick, Jr. Chair and Distinguished Scientist, University Hospitals Harrington Heart & Vascular Institute; Director, Case Cardiovascular Research Institute; Professor of Medicine at Case Western Reserve University School of Medicine – changed Dr. Narla’s career path and allowed him to follow his interests in the field of cancer therapeutics.

Career Transformation

Dr. Jain and Jonathan S. Stamler, MD, Director, Harrington Discovery Institute at UH Case Medical Center; Director of the Institute for Transformative Molecular Medicine at Case Western Reserve University and UH Case Medical Center; Robert S. and Sylvia K. Reitman Family Foundation Distinguished Chair in Cardiovascular Innovation at University Hospitals Harrington Heart & Vascular Institute and Case Western Reserve University School of Medicine; and Professor of Medicine and of Biochemistry at Case Western Reserve University School of Medicine, recruited Dr. Narla to the hospital system and Case Western Reserve University School of Medicine from Mount Sinai School of Medicine in New York. Dr. Narla, now an assistant professor in the Institute for Transformative Molecular Medicine, has the distinction of being named the inaugural Harrington Distinguished Scholar (Early Career Award) of the Harrington Discovery Institute.
“The Harrington Discovery Institute is an unusually forward-thinking and visionary project,” Dr. Narla says. “With the Harrington Discovery Institute, you have the best of both worlds – fundamental science and translational research, and drug development.”

Designing Tomorrow’s Treatments from Yesterday’s Drugs

Dr. Narla’s laboratory focuses on the identification and characterization of genes and pathways involved in cancer metastasis, the spread of cancer to sites in the body away from its original location. Through his study of the functional role of a specific tumor-suppressor gene, Dr. Narla and his team identified new signaling pathways that this gene family regulates, providing new insights into cancer diagnosis and treatment. The team found that two tumor-suppressor genes are turned off as cancer spreads through the body.

By using a combination of two existing approved drugs – erlotinib, a targeted cancer drug, and trifluoperazine, a medication used to treat psychotic disorders – the team developed an understanding of the properties that turn these critical genes back on. When the genes are turned on, they initiate tumor cell suicide, and cancer cannot spread.

“We’re now designing new drugs from old drugs to keep the anti-cancer properties of these drugs, while removing the side effects that have limited their potential use in cancer patients,” Dr. Narla explains.

Therapy on the Fast Track

Dr. Narla’s project was the first selected for funding through BioMotiv, the for-profit accelerator company associated with the Harrington Discovery Institute. He says that the team could be filing paperwork to begin clinical trials as early as this year and should have an initial idea about the safety and efficacy of the drugs by the end of 2014.

Dr. Narla credits the Harrington Discovery Institute with introducing him to some of the nation’s most accomplished medical innovators, leaders in the pharmaceutical and biotechnology industries, health care entrepreneurs and philanthropists. He considers the support of the Harrington Discovery Institute “transformative” for a physician-scientist’s career.

“I would never have embraced this drug development project if not for the support of the Harrington Discovery Institute,” Dr. Narla says. “It’s the best thing that’s ever happened to me as a physician-scientist.”

The Harrington Distinguished Scholars Program

The Harrington Distinguished Scholars Program supports physician-scientists seeking to move their research into therapies that will improve patients’ lives. Selected physician-scientists are invited to practice medicine at University Hospitals Case Medical Center and to hold a faculty position at Case Western Reserve University School of Medicine.

As a Harrington Distinguished Scholar, physician-scientists with potential breakthroughs can tap into grant funding and a peer network of innovators and mentors within the Harrington Discovery Institute at UH Case Medical Center to support their discovery efforts. Over the next decade, the Harrington Discovery Institute will recruit 10 to 20 physician-scientists at varying points in their careers who have an interest in advancing their science into commercially available drug therapies to conquer disease and relieve human suffering.
A cure for cancer. A drug that prevents Alzheimer’s disease. Better treatment for heart disease. The need for new, more effective treatments for humankind’s most devastating diseases is overwhelming.

Hundreds of remarkable new scientific discoveries are made every year that have the potential to become treatments. But the traditional drug development system too often fails to bridge the gap between scientific discovery and a marketable drug, and some of the most promising discoveries are left lingering in the void.

The Harrington Discovery Institute Scholar-Innovator Grant Program steps in to fill that void by carrying some of the most promising scientific breakthroughs across the “Valley of Death” between discovery and commercialization. Financial support combined with the expert mentorship and guidance provided by the Innovation Support Center will allow the Harrington Scholar-Innovators to take the next important steps in transitioning their groundbreaking discoveries from laboratory bench to patient bedside.

The Harrington Scholar-Innovators are associated with some of the most prestigious academic medical centers in the United States, from coast to coast, including University Hospitals Case Medical Center. Their educational credentials are impeccable, distinguished by medical degrees and postdoctoral training at leading academic and medical institutions around the world. Their consistent dedication to scientific investigation has yielded revolutionary discoveries that have the potential to be developed into the breakthrough medical treatments of the 21st century.

The first Harrington Scholar-Innovators, introduced on the following pages, were selected from more than 130 applicants representing 53 institutions. Each Harrington Scholar-Innovator receives funding of up to $100,000 a year for two years and open access to the scientific and business resources of the Harrington Discovery Institute at UH Case Medical Center and the Innovation Support Center.

In the tradition of Marie Curie, Jonas Salk and Edward Jenner, the Harrington Scholar-Innovators represent the epitome of the modern day physician-scientist. Motivated to change the status quo in medicine through discovery and innovation, their inventiveness, creativity and exceptional scientific ability exemplify the core values of the Harrington Discovery Institute.
The Harrington Scholar-Innovators are associated with some of the most prestigious academic medical centers in the United States, from coast to coast.
Alzheimer’s disease, with its slow descent into mental, emotional and psychological oblivion, is perhaps one of the most feared diseases of the 21st century. To Marc I. Diamond, MD, a neurologist and the David Clayson Professor of Neurology at Washington University School of Medicine, it’s also one of the most fertile areas for translational research.

In his clinical practice, Dr. Diamond regularly treats patients with neurodegenerative diseases and sees their effects on patients and families. “Diseases like Alzheimer’s, Parkinson’s and Lou Gehrig’s are devastating for those they affect, not only the person with the disease but also their loved ones, who watch their steady decline,” he says. “Better diagnostic tests and effective treatments are desperately needed.”
Dr. Diamond’s inspiration derives not only from his patients but also from his father, Ivan Diamond, MD, PhD, researcher and founding director of the Ernest Gallo Clinic and Research Center at the University of California, San Francisco. “My dad impressed upon me the excitement and joy of life as an academic physician, and the worthiness of the work,” he says.

Devising a Game-Changer

Since joining the Department of Neurology at Washington University in 2009, Dr. Diamond has concentrated his research on neurodegenerative diseases. His laboratory was responsible for a major breakthrough in understanding the development of neurodegenerative diseases like Alzheimer’s with the discovery that pathologic proteins in these diseases propagate pathology between cells, just like prion protein.

Building on that discovery, he now is exploring the development of antibodies that can target these pathologic proteins and block their spread through the brain. “If this approach is successful, it could be a game-changer in Alzheimer’s treatment,” he says. “Anything that would significantly slow down the disease, let alone cure it, would have enormous impact on our society.”

Always considering the practical clinical application of his discoveries, Dr. Diamond sees the need for a screening tool that could detect these protein pathogens before they have a chance to cause any harm to the brain. So far, he has discovered a way to detect the pathogens in spinal fluid and blood prior to the onset of dementia.

Exploring the Options

“It’s early in the discovery process, but I am very excited by the potential implications of this work, although the corollary is that once we can detect the disease at a preclinical stage, we need to have a therapeutic intervention available,” he says.

That, he notes, is the beauty of the Harrington Discovery Institute at University Hospitals Case Medical Center. “The Harrington Discovery Institute model not only provides funding, it also connects us with the expertise to bring discoveries to a point where they can be translated to patient care.”

Dr. Diamond’s next steps will be developing antibodies that are more effective at interfering with the pathologic process and refining the screening technique. Support from the Harrington Discovery Institute will give him the flexibility to explore different approaches, he says. “It is helping me go in directions that promise to be the most productive – and the most exciting.”

“My dad impressed upon me the excitement and joy of life as an academic physician, and the worthiness of the work.”
“The excitement of discovery drives me on a daily basis,” says Roger A. Greenberg, MD, PhD, researcher in the Abramson Family Cancer Research Institute and associate professor in the University of Pennsylvania’s Perelman School of Medicine. That excitement paired with years of diligent research at the laboratory bench has led Dr. Greenberg to identify the molecular basis for a potential new cancer treatment.

Targeting Hereditary Cancers

Dr. Greenberg has discovered an enzyme that is required to repair certain types of DNA damage that occur during the development of hereditary breast and ovarian cancer. He believes that he can inhibit this enzyme to create irreparable DNA damage in the cancer cells, causing the cells to die. This mechanism could be the foundation for new, more effective chemotherapy drugs.

The challenges inherent in any exploration of novel therapeutic approaches to cancer don’t discourage Dr. Greenberg. In fact, the challenges intensify his interest in the research. “I think it’s exciting to work on something that’s novel, that’s uncharted territory,” he says. He plans to apply his Harrington Discovery Institute Scholar-Innovator grant to navigate through that uncharted territory with additional work on refining the use of the enzyme against breast and ovarian cancer.

Dr. Greenberg’s dedication to understanding the molecular basis of disease dates back to his undergraduate years at Haverford College in Pennsylvania. As part of a Howard Hughes Medical Institute program for interdisciplinary research, he had his first taste of scientific research.

Working for several years after graduation as a scientist with DuPont-Merck Pharmaceuticals piqued his interest in drug development and medicine, leading to his decision to attend medical school. But it was his work with renowned cancer

ROGER A. GREENBERG, MD, PHD
HEREDITARY BREAST AND OVARIAN CANCER

“The support provided by the Harrington Discovery Institute is very unique and very special.”
researcher David M. Livingston, MD, at Harvard’s Dana-Farber Cancer Institute after earning his medical degree that ultimately shaped his career as a physician-scientist.

“Dr. Livingston’s focus is on the molecular pathogenesis of breast and ovarian cancer. The four years I spent with him deeply inspired my work at U Penn,” Dr. Greenberg says. Working with Dr. Livingston, Dr. Greenberg developed his research skills along with a special interest in DNA repair processes and their potential relationship to cancer treatment.

Laying the Groundwork

Now, after more than a decade of research, Dr. Greenberg believes that his work is at a crucial stage. Through the relationship-building opportunities that the Harrington Discovery Institute at University Hospitals Case Medical Center offers the Harrington Scholar-Innovators, he hopes to lay the groundwork for translating his laboratory discoveries into a powerful new cancer treatment.

“To develop the necessary expertise to do this on our own would be tremendously time-consuming, difficult to assemble and prohibitively expensive,” he notes. “The support provided by the Harrington Discovery Institute is very unique and very special.”

It’s important to Dr. Greenberg that the Harrington Discovery Institute Scholar-Innovator grant allows him free rein to follow his research wherever it leads, into that uncharted territory. “I get to apply what I love to do, which benefits humankind and is exciting on an intellectual level,” he says. “That is what really makes this very rewarding.”

“I think it’s exciting to work on something that’s novel, that’s uncharted territory.”
In the 25 years since his graduation from medical school at the University of California, San Francisco, Geoffrey C. Gurtner, MD, FACS, a plastic surgeon and professor at Stanford University, has earned a reputation as a physician, a scientist and an entrepreneur. He maintains a busy plastic surgery practice, is engrossed in leading-edge research in wound healing, has authored nearly 200 articles in the medical literature and brought innovative products to market in the diverse fields of aesthetic plastic surgery, cardiovascular surgery and wound healing.

**Starting with the Basics**

To Dr. Gurtner, translational research – “where surgery meets science,” in his words – offers the opportunity to make a difference through discovery. “In medicine you really have to go back to the lab and understand what causes a problem and try to brainstorm a solution or better ways of doing things,” he explains. “My research has always been very translationally focused on clinical needs that are unaddressed by current technologies, companies or drugs.”
In his latest research, Dr. Gurtner and his team at Stanford University have discovered a negative correlation between high blood sugar and tissue regeneration and fibrosis. He believes that this irreversible disruption of the healing process at the molecular level is responsible for the development of nonhealing wounds in patients with diabetes.

With support from the Harrington Discovery Institute at University Hospitals Case Medical Center, Dr. Gurtner hopes to translate this research into a prophylactic treatment that would prevent wounds in people with diabetes, paraplegics and other patient populations prone to chronic wounds. This is a field where he believes research lags behind the clinical need. In particular, he says, “It is the patients that I deal with who have seemingly unsolvable problems that are the real imperative.”

In parallel with his work on the molecular basis for chronic wounds, Dr. Gurtner is developing a skin patch delivery system for his eventual wound-prevention drug. Ultimately, he aims to have 10,000 patches produced for testing in clinical trials.

Taking a Risk
He describes his research as innovative and high risk – two descriptors that can spell sudden death in the land of funding support. “This is an area that can only be funded by an organization such as the Harrington Discovery Institute, where it’s not necessarily just hard-nosed businessmen worried about the bottom line,” Dr. Gurtner says. That kind of thinking leads only to small, incremental change, he adds. “If we only listened to the business perspective, we would still be going across the sea in steamships.”

Despite years of personal experience in securing start-up funding and navigating through the maze of regulations on the way to commercializing a discovery, Dr. Gurtner welcomes the expertise of the Harrington Discovery Institute’s advisory boards. “Having an organization that says translation is important, that they will help you figure out the regulatory pathway for the drug, device or biologic and, at a minimum, has a network of people willing to work on it – that is pretty unique.”

“My research [is] very translationally focused on clinical needs that are unaddressed by current technologies, companies or drugs.”
Ask Richard N. Kitsis, MD, professor and director of the Wilf Family Cardiovascular Research Institute at Albert Einstein College of Medicine, about the challenges and pitfalls he expects to encounter with his research on a new heart drug, and his answer is unexpected. “I think about the challenges,” he says, “but I’m an optimist, so my approach is more ‘Damn the torpedoes, full steam ahead!’”

Taking Aggressive Action

That no-holds-barred approach to scientific investigation has led to his discovery of a specific molecular compound that inhibits the death of heart muscle. Translated into a drug that could be given to patients having a heart attack, it has the potential, Dr. Kitsis believes, to limit the amount of dead heart tissue caused by the attack.

This is critical, he explains, because a nonfatal heart attack that causes extensive damage to the heart muscle typically leads to congestive heart failure. Limit the damage, he says, and the incidence of congestive heart failure drops. End result – a healthier population and lower medical costs.

Dr. Kitsis’ passion for helping people with heart attack has its roots in his personal life. “My father had a heart attack when I was 13. That made a big impression on me, although I probably didn’t realize it at that time,” he recalls.

Ten years later, as a resident at Massachusetts General Hospital and the Boston VA Medical Center, he discovered that he was fascinated by cardiovascular medicine. His interest in the clinical side of heart disease continued during his fellowship in cardiology at Albert Einstein College of Medicine. He was appointed to the faculty in 1991, specializing in cardiovascular medicine, and was named Chief of Cardiology in 2005.

In recent years, Dr. Kitsis has given up his clinical leadership role to direct the newly endowed Wilf Family Cardiovascular Research Institute and focus on his research. Now, he believes, his work on the molecular mechanisms of cell death and their roles in heart disease is at a critical juncture.
Zeroing In On the Target

“We now know that cell death during a heart attack is regulated,” he explains. “We have identified a compound that we know inhibits heart muscle death. With the Harrington Discovery Institute Scholar-Innovator grant, we can determine its molecular target in the cell and how it interacts with that target.”

From there, the next steps will be to modify that compound to improve its effectiveness and, eventually, move it into the drug development pipeline. At that stage, his discovery shifts from academia to the business arena, requiring the resources of a drug company to bring it to market. The opportunities offered by the Harrington Discovery Institute at University Hospitals Case Medical Center to develop relationships with drug companies that share his vision was one of the reasons he applied for a Harrington Scholar-Innovator grant, Dr. Kitsis shares.

The path from laboratory bench to the patient’s bedside is a long one, but a journey with its own rewards, he says. “There are a series of little eureka moments along the way. You can’t build a wall in one step, but every time you put a brick in the wall – those little eurekas – it’s exciting.”

“My father had a heart attack when I was 13. That made a big impression on me.”
As a scientist, Wolfgang B. Liedtke, MD, PhD, associate professor and faculty of the Center for Translational Neuroscience at Duke University School of Medicine, understands pain at the molecular level. As a physician, he understands it on the human level.

Recruited by Duke in 2004 based on the impact of his 2000 discovery of the TRPV4 ion channel, Dr. Liedtke was encouraged to practice neurology and pursue his own research in this specialty. He embarked on a study of pathological pain at the molecular level and within two years had organized a clinic focusing on patients suffering from trigeminal nerve pain, a chronic pain disorder.

“I was caught up by the suffering of people with this condition,” Dr. Liedtke says. “I felt an enormous calling to make progress on their behalf.”

Unraveling the Causes

Inspired by his patients to this day, he seeks to expand the understanding of chronic pain mechanisms at the molecular level. The ultimate goal, he explains, is to translate understanding to clinical application.
“We know that this TRPV4 ion channel allows calcium ions to enter sensory nerve cells, which can lead to reprogramming,” he explains. “Reprogramming of sensory nerve cells is a likely co-contributor to chronic pain.”

He hopes to identify specific agents that can block TRPV4’s function so that the channel in the nerve is unable to conduct ions. Blocking this critical step would interrupt the cell reprogramming and possibly the chronic pain response.

Dr. Liedtke is encouraged by published papers from other researchers that have documented various aspects of TRPV4’s function in pain. “My hope is that I will be able to add to the understanding of the pain mechanism and how the nervous system is damaged so that we can control the changes more rationally,” he says.

Planning for the Future

Having trained during his medical internship, residency and fellowship with leaders in the fields of neurology, psychiatry, neuropathology and molecular biology in Zurich, Paris and New York, Dr. Liedtke learned to dream big. Eventually he hopes to organize his clinical experience with more than 500 patients with trigeminal pain disorders into a translational research study and share the findings.

In the immediate future, the Harrington Discovery Institute Scholar-Innovator grant will help Dr. Liedtke move his research closer to Phase I clinical trials, studies in small groups of patients that evaluate a new treatment’s safety. “The grant will be an enormous boon to our efforts,” he says.

A scientist-physician who thinks in multiple directions at once, he also is considering how to harvest cells from patients and coax them in the laboratory into induced pluripotent stem cells, then nerve cells that could be used in medical applications. “The end result would be genomic personalized medicine to augment treatment of pathological pain,” he explains. “If we could develop such a system, it could teach us – amongst other things – who responds to what drugs.”

After more than two decades as a physician and researcher, Dr. Liedtke is still gripped by the power of scientific investigation. “On the canvas of insight, mostly blank, you can start painting using the scientific method,” he says. “The poor state of the human mind is the only limitation.”
For Sanford D. Markowitz, MD, PhD, an oncologist at University Hospitals Seidman Cancer Center and the Markowitz-Ingalls Professor of Cancer Genetics at Case Western Reserve University School of Medicine, cancer research has a personal dimension. Early in his medical career, his father developed colon cancer, inspiring in Dr. Markowitz a desire to fight back against this disease.

“Anyone who has experienced the acute terror of having cancer strike a family member, who has dreaded that every ache, pain or ailment was the beginning of the end, understands this desire to do something to make a difference,” he says. Now, years after his father’s illness, the patients he treats in his oncology practice provide a continuing source of motivation. “I’ve seen patient after patient, and I wanted to be able to help but lacked the means to do so,” he adds.

Identifying a Genetic Control

Dr. Markowitz, who heads the cancer genetics program in the Case Comprehensive Cancer Center at Case Western Reserve University, is dedicated to understanding the genetic basis for colon cancer as the key to developing better treatments. He and his team have identified a genetic “switch” that controls cell division and tissue growth in colon cancer. Theoretically, turning off this genetic switch should prevent a tumor from growing. Turning it on potentially would promote tissue growth, a situation that could be useful in promoting new tissue growth following organ transplant.

So far, he and his team have tested more than 100 compounds and identified two specific compounds that regulate the gene switch – one that turns it off and one that turns it on. Laboratory tests of the “on” compound have shown some success in tissue regeneration.

With the Harrington Discovery Institute Scholar-Innovator grant, Dr. Markowitz plans to continue testing the compound in animal models, ultimately hoping it will have application in the treatment of colitis and inflammatory bowel disease as well as liver and bone marrow transplantation. To conduct this next stage of research, Dr. Markowitz first will develop an analog of the compound that has a longer half-life so that therapeutic blood levels can be maintained longer.
Beyond the Lab

As exciting as he finds the basic research process, Dr. Markowitz is keenly aware of the need to translate scientific discoveries into commercially viable treatments — and the barriers to making that happen. “The biggest challenge for any academic laboratory is to get beyond the lab and develop a therapy,” he explains.

“You need collaborators, pharmaceutical companies, biotechnology companies that can produce compounds according to FDA safety standards. In general, academicians do not have access to those kinds of organizations.”

The Harrington Discovery Institute at University Hospitals Case Medical Center, with its two advisory boards and relationships with the pharmaceutical industry and venture investors, does have that access. “The contact with experts who can help ensure that a new treatment is deliverable, stable and meets federal safety standards can make a critical difference in whether a new drug is successful,” Dr. Markowitz says. “By connecting academics with industry experts, the Harrington Discovery Institute is giving our ideas a fighting chance to succeed.”

“By connecting academics with industry experts, the Harrington Discovery Institute is giving our ideas a fighting chance to succeed.”
Scott A. Oakes, MD, and Feroz R. Papa, MD, PhD, associate professors at the University of California, San Francisco (UCSF), prove the truth of the old adage “Two heads are better than one.” Coming from two different perspectives and trainings – Dr. Oakes is a pathologist in the UCSF Diller Family Comprehensive Cancer Center; Dr. Papa is an endocrinologist within the UCSF Diabetes Center – the two put their heads together to discover new details about the causes and mechanisms of cell death.

Converging on a Fresh Approach

“We were working on the same problem from two different ends – Feroz was studying one end of the problem and I was studying the other end,” Dr. Oakes says. His research focuses on the mechanism for cell death in response to cell injury. Dr. Papa is studying how the cell detects stress and transmits those signals to the cellular death-promoting machinery. Eventually, they hope these two vantage points will converge on a new understanding of diseases that are caused by cell degeneration under unchecked cell stress, such as diabetes, Alzheimer’s disease, Parkinson’s disease and Lou Gehrig’s disease.

“Our work and passions brought us together, and Scott and I developed a collegial relationship that provides a sense of fulfillment and gratification that adds to the work that we do,” Dr. Papa says. The two researchers share resources, research teams and responsibilities. “That spirit of camaraderie, that working relationship has trickled down to the people that work for us,” he adds.
Drs. Oakes and Papa have been working together since 2007 and are making progress at “saving cells” that they believe has significant potential for translation into clinical care. They have identified IRe1, a protein that plays a critical role in many biological processes, as a regulator of cell fate. IRe1 is a cellular stress sensor that normally protects cells from death when stress levels are low and manageable. But, under prolonged conditions of high cellular stress, it can activate a series of biologic events that actually cause cell death instead.

**Survival Under Stress**

Through collaboration with chemist Dustin Maly, PhD, an associate professor at the University of Washington, the researchers have identified several IRe1 inhibitors that can tilt the cellular balance toward survival under stress conditions. “We expect that these compounds will be powerful tools to investigate connections between cell stress and cell death,” Dr. Papa explains. “We currently are advancing these compounds through medicinal chemistry to make them more drug-like and useful for animal and preclinical studies.”

Their long-term goal is to develop new drugs that reduce cell stress and cell death to treat many cell-stress-related degenerative diseases. Their target list includes the neurodegenerative diseases and other diseases of cell loss such as type 2 diabetes, as well as certain types of cancer in which cells fail to die appropriately in response to stress. With the basic science behind their therapeutic vision steadily gaining traction, Drs. Oakes and Papa are positioned to take advantage of the resources that the Harrington Discovery Institute at University Hospitals Case Medical Center can offer for moving their discoveries from bench to bedside.

“We were working on the same problem from two different ends – Feroz was studying one end of the problem of cell death, and I was studying the other end.”

– Dr. Scott A. Oakes

“We expect that these compounds will be powerful tools to investigate connections between cell stress and cell death.”

– Dr. Feroz R. Papa
Jonathan D. Powell, MD, PhD, an oncologist and associate professor of oncology at The Johns Hopkins University School of Medicine, set his sights on a career that combined medicine and research while he was still an undergraduate at Dartmouth College. “I entered Dartmouth as a pre-med student and planned to go to medical school, but participating in research as an undergraduate slightly changed my plans,” he explains.

His desire to integrate medicine with research led him to pursue a dual MD/PhD degree at Emory University instead of the MD degree he originally planned. After finishing both degrees at Emory, Dr. Powell completed a residency at The Johns Hopkins University followed by a clinical fellowship at Harvard. He then went on to a post-doctoral fellowship in immunology at the National Institutes of Health in Bethesda, Md., an experience that helped set a direction for his research that continues today with his studies of T-cell function in his lab at Johns Hopkins.

Following Where the Research Leads

That work recently has led Dr. Powell in still another direction. He was conducting basic research into the role of T-cells in the body’s immune system using laboratory mice. During the course of these studies, Dr. Powell and his team noted that a group of mice with genetically altered immune cells became obese.

Analysis revealed that the obese mice were generating brown adipose tissue, a type of fat that plays a role in regulating body weight and metabolism, including glucose tolerance and insulin sensitivity – two important factors involved with the development of diabetes. The mice with the “brown fat” were resistant to type 2 diabetes and exhibited favorable blood levels of cholesterol and triglycerides.
“By studying the immune system, we believe we have uncovered a potentially new approach to treating diabetes.”

“By studying the immune system, we believe we have uncovered a potentially new approach to treating diabetes,” Dr. Powell says. “Our finding is a nice example of how, by supporting basic research, unexpected spin-offs into translational research can emerge.”

The excitement of these unexpected new findings has led Dr. Powell and his team to pursue this new line of inquiry further, a temporary departure from their typical research in immunology. Dr. Powell believes that his discovery could have a significant impact on treating diabetes, obesity and heart disease.

Opening Doors to a New Approach

His team already has identified a candidate gene that they believe likely promotes the creation of brown fat. “If this turns out to be the case, it might lead to the development of a completely novel approach to treating type 2 diabetes and, potentially, obesity and hyperlipidemia,” Dr. Powell says.

He sees the Harrington Discovery Institute at University Hospitals Case Medical Center as offering him a unique opportunity to rapidly develop this exciting line of inquiry. “Not only does it provide funding through the Harrington Scholar-Innovator grant to support our experiments,” he says, “it also provides the scientific and business resources to develop our findings into a drug.”
Larry S. Schlesinger, MD, professor and chair of the Department of Microbial Infection and Immunity at The Ohio State University, has devoted his career to studying some of the tiniest organisms that create the biggest impact on humans. As director of the Center for Microbial Interface Biology, Dr. Schlesinger is an internationally known expert in tuberculosis and other microorganisms that manipulate the lung’s natural defenses.

He considers infectious diseases like tuberculosis the ultimate challenge for a physician-scientist. “Infectious diseases have shaped mankind more than any other type of disease,” he explains. “Now, as the world is getting smaller, we have the problem of adaptive organisms to solve. We desperately need more innovative approaches to controlling infections.”

Dr. Schlesinger’s career path was set early in his career when he worked in a research lab while in medical school at Rutgers. “I discovered I love ‘following that thought,’ investigating why events occur,” he says. “Research is in my blood. I love discovery, it’s exciting to me.”
Laying the Foundation

Later, as an internal medicine intern at the University of Michigan, he developed an interest in understanding what underlies human health and disease. His passion for research, interest in the causes of disease and a deep-seated love for people all came together during his postgraduate study at the University of California, Los Angeles. As a fellow, he delved into researching leprosy and eventually tuberculosis, developing laboratory models relevant to human health.

That was the jumping-off point for further tuberculosis research, which eventually propelled him to the University of Iowa. After 11 years at Iowa, a desire to build a larger research team, focusing on translational research, launched his decision to move to Ohio State and establish the Center for Microbial Interface Biology.

At the center, Dr. Schlesinger and his team are developing a two-pronged therapeutic approach to tuberculosis – discovering compounds that attack the TB microbe and also modulate the body’s inflammatory response to it. “I am suggesting new bifunctional targets for treating TB,” he explains.

Translating Science into Treatment

The Harrington Discovery Institute Scholar-Innovator grant will impel his work into the next phase, providing for research in animal models, formulation of the drug delivery system and imaging to evaluate the drug’s disposition in tissues. At that point, he believes his work will be of great interest to drug companies.

The relationship that the Harrington Discovery Institute at University Hospitals Case Medical Center will foster among physician-scientists and pharmaceutical companies was one of the unique features of the grant that piqued Dr. Schlesinger’s interest in making application. “My passion is drug discovery,” he says. “We have an enormous opportunity to translate biologic pathways into therapeutics, but it requires a partnership between academic institutions and the drug companies. This is a tremendous chance to engage with investigators with an equal passion for new therapeutics and connect with industry.”

In becoming part of the Harrington Discovery Institute, Dr. Schlesinger feels that he has connected with a team that understands him as well as his work. “The Harrington grant application specified they were seeking physician-scientists who are creative, passionate and interested in drug development,” he says. “They wrote who I am.”
Physician, molecular geneticist, philosopher, composer – Robert B. Wilson, MD, PhD, professor and pathologist at the Hospital of the University of Pennsylvania, is a unique blend of scientist and artist.

As an undergraduate at Brown University, “I was thoroughly into music, but I became enamored of science and medicine,” Dr. Wilson recalls. He decided to stay a fifth year at Brown to further his music and philosophy studies and learned he also could complete a biochemistry degree by taking just two more science classes. At the end of his fifth year, he graduated with degrees in music and biochemistry, both with High Honors.

His eclectic undergraduate pursuits yielded not only a collection of original musical compositions but also a place in the MD/PhD program at the University of Pennsylvania. He completed his training there with a residency in clinical pathology and a fellowship in transfusion medicine, culminating in a faculty appointment in molecular pathology.

Taking a New Direction

The discovery of microRNAs in the early 1990s fired his imagination as he considered the possible therapeutic uses of these short-chain nucleic acids. By regulating gene expression, microRNAs play a key role in diverse biological processes, including cell proliferation, differentiation and death.

Dr. Wilson's first work with microRNAs investigated their potential therapeutic application in Friedreich’s ataxia, a rare neurologic condition on which he is an internationally recognized expert.

For the past year, Dr. Wilson and his team have turned their attention to the potential to use shRNAs, artificial versions of microRNAs, in cancer treatment. They are searching among three million shRNA sequences to identify the ones that specifically suppress cancer cell growth. The work is painstaking, dealing with 30 million lines of data on spreadsheets, repeating tests, identifying target gene sequences.
Opening the Door

Dr. Wilson is driven to find shRNAs that are toxic to cells that lack a tumor suppressor. Such a discovery could lead to small-RNA therapeutics or identify possible therapeutic targets to disrupt cancer cell growth and multiplication. To date, he and his team have found shRNA sequences that may specifically inhibit prostate cancer cells.

“It opens the door to the possibility of a personalized mix of drugs for prostate cancer determined by each tumor’s genetic profile,” Dr. Wilson explains. “Another possibility would be using an shRNA to enhance the specificity of current drugs to make them more curative or less toxic.”

Although Dr. Wilson characterizes himself as “an empirical skeptic,” he believes that his team’s discovery is worth taking further. His Harrington Discovery Institute Scholar-Innovator grant will help him to optimize his approach, which he anticipates eventually will lead to the discovery of shRNAs specifically toxic to cancer cells. Although this work is still in its early stages, he is convinced that shRNAs hold the potential to yield a breakthrough in cancer treatment.

That possibility, he says, is what makes his work worthwhile. “Bringing knowledge from basic science in the laboratory to making a difference in human health,” he says. “That’s what gets me up in the morning. I fundamentally love what I am doing.”

“As an undergraduate, I became enamored of science and medicine.”
As the centerpiece of the nonprofit Harrington Discovery Institute at University Hospitals Case Medical Center, the Innovation Support Center makes available powerful resources to physician-scientists to cross the “Valley of Death” and optimize the development of therapeutics that will cure disease and save lives.

Under the direction of Perry B. Molinoff, MD, professor of Pharmacology at the University of Pennsylvania, the Innovation Support Center provides the infrastructure to support Harrington Discovery Institute Scholar-Innovators with the goal of maintaining momentum and increasing the number of new, clinically useful drugs. Each Innovation Support Center project plan identifies the most crucial technical issues that will impact commercial success and forges relationships among inventors, industry experts, investors and entrepreneurs essential to the drug development process.

Bridging the Gap

“A real crisis exists in the pharmaceutical industry today,” says Dr. Molinoff, who has more than 30 years of experience in both the academic and industrial sectors. “There is a dearth of new projects and newly approved drugs that will not replace the income lost due to expiring patents. Many promising discoveries are made in the laboratories of academic investigators, but getting the support or knowledge that you need to develop those discoveries into drugs is very difficult.”

The Innovation Support Center bridges the gap between highly innovative research and early-stage advancement of commercially viable drug development projects. It achieves its mission by:

- Advising physician-scientists on crucial elements of clinical and commercial development, assessing commercial potential and connecting Harrington Scholar-Innovators with a network of industry experts;
- Improving access to institution-based and other technology resources through collaborative, multi-institution alliances;
- Identifying and securing funding to bridge projects across the critical translational threshold from laboratories to commercialization vehicles;
- Managing projects across participating laboratories, institutions and commercial partners;
- Identifying the most efficient vehicles to advance projects beyond academia, including company creation, sponsored research agreements and intellectual property (IP) augmentation.
An eight-member Advisory Board comprised of veteran investigators – all of whom have in-depth experience in the pharmaceutical industry – offers mentorship in drug development. In addition, the Innovation Support Center provides market assessments and helps to devise commercialization strategy, provides IP and regulatory advice, and supports grant preparation and the pursuit of additional funding.

Making Critical Connections

The Innovation Support Center also connects the Harrington Scholar-Innovators with a national consortium of academic medical centers and commercial research organizations that can facilitate high-throughput screening, medicinal chemistry, preclinical development, pharmaceutical development and collaboration with commercial partners. The consortium can provide expedited access to core facilities and resident expertise.

“Many entities provide grants, awards and fellowships. Almost none include the kind of support we’re providing to help investigators actually develop their projects,” Dr. Molinoff notes. “We have a laundry list of services we can provide that will vary from investigator to investigator.”

In addition to his role as director of the Innovation Support Center, Dr. Molinoff is on the BioMotiv Advisory Board. In his previous position as Vice Provost for Research at the University of Pennsylvania, he developed linkages between the university and industry to enable technology transfer from university laboratories to commercial application. He previously served in leadership positions at the biopharmaceutical company Palatin Technologies and the Bristol-Meyers Squibb Pharmaceutical Research Institute.

“Getting the support or knowledge that you need to develop…discoveries into drugs is very difficult.”
The journey that takes a scientific discovery from laboratory bench to patient bedside can be long, arduous and fraught with potential roadblocks and pitfalls. Navigating it successfully calls for perseverance, fortitude and expert guidance.

HARRINGTON DISCOVERY INSTITUTE SCIENTIFIC ADVISORY BOARD

SCIENTIFIC ADVISORY BOARD MEMBERS BOAST AN IMPRESSIVE RECORD OF CONTRIBUTIONS TO ADVANCING PATIENT CARE.

Jonathan S. Stamler, MD, Director, Harrington Discovery Institute; Robert S. and Sylvia K. Reitman Family Foundation Distinguished Chair in Cardiovascular Innovation at University Hospitals Harrington Heart & Vascular Institute and Case Western Reserve University School of Medicine; Professor of Medicine and of Biochemistry, Case Western Reserve University School of Medicine; member, BioMotiv Board of Managers and Advisory Board

- Discovered protein S-nitrosylation and how nitric oxide works in the body, which has advanced the work of thousands of researchers on promising new treatments for asthma, heart failure, high blood pressure, cancer, Alzheimer's disease and other diseases
- Co-founded five drug companies
- Holds more than 125 patents

Irwin Fridovich, PhD, James B. Duke Professor Emeritus of Biochemistry, Duke University

- Discovered the enzymes superoxide and superoxide dismutase, which anchored the fields of antioxidant biology, aging and environmental toxicology
- Founded Incara Pharmaceutical’s catalytic antioxidant program
- Holds more than 100 patents

David Ginsburg, MD, James V. Neel Distinguished University Professor of Internal Medicine and Human Genetics; Warner-Lambert/Parke-Davis Professor of Medicine; Member of the Life Sciences Institute at the University of Michigan Medical School; Howard Hughes Medical Institute Investigator

- Identified several genes in the clotting pathway, including the gene for von Willebrand factor and other inherited versions of coagulation diseases
- Member of the Scientific Advisory Boards for Portola Pharmaceuticals and Catalyst Biosciences; member of the Board of Directors, Shire Plc
- Holds numerous patents

William G. Kaelin Jr., MD, Professor of Medicine, Harvard Medical School; Howard Hughes Medical Institute Investigator, Dana-Farber Cancer Institute; Senior Physician, Medicine, Brigham and Women’s Hospital

- Uncovered molecular pathways that led to the development of two kidney cancer drugs approved by the U.S. Food and Drug Administration
- Member of Scientific Advisory Board of Nextech Venture Ltd., ArQule Inc., TRACON Pharmaceuticals, Inc., Traversa Therapeutics, Inc.
- Member of Board of Directors, Eli Lilly & Co
The Harrington Discovery Institute Scientific Advisory Board, with a sum total of more than 175 years of drug discovery experience among its seven members, provides the knowledge and experience to guide the Harrington Discovery Institute Scholar-Innovators, Distinguished Scholars and Foundation Scholars through the difficulties and challenges to successful commercialization of their discoveries.

The renowned physician-scientists who make up the Scientific Advisory Board have aligned with the Harrington Discovery Institute at University Hospitals Medical Center because they share its vision for accelerated drug development that will lead to transformational patient care. Under the leadership of Jonathan S. Stamler, MD, Director of the Harrington Discovery Institute, Scientific Advisory Board members evaluate research and preclinical studies to identify those projects best suited for commercialization.

As an elite team comprising some of the nation’s most accomplished and connected medical innovators, the national advisory board will build the Harrington Discovery Institute’s physician-scientist community across the country and advance academic medicine’s involvement in drug discovery and development.

Andrew R. Marks, MD, Chairman, Department of Physiology and Cellular Biophysics, Columbia University Medical Center; Founding Director, Wu Center for Molecular Cardiology; Professor, Physiology and Cellular Biophysics, Columbia University Medical Center
- Led research that resulted in development of the drug-eluting coronary stent and a first-of-its-kind therapy for treatment of heart failure
- Founded ARMGO Pharma, Inc. and chairs its Scientific Advisory Board
- Holds 20 patents

Charles L. Sawyers, MD, PhD, Howard Hughes Medical Institute Investigator; Marie-Josée and Henry R. Kravis Chair and Chairman, Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center
- Discovered the signaling pathways that drive cancer cell growth, leading to new treatment options for chronic myeloid leukemia, prostate cancer and glioblastoma
- Co-founded and serves as Scientific Advisor, Aragon Pharmaceuticals, Inc. and co-founder, Agensys
- Played key role in clinical development of imatinib (Gleevec®) and dasatinib (Sprycel®)

Solomon H. Snyder, MD, DSc, DPhil, Distinguished Service Professor of Neuroscience, Pharmacology, and Psychiatry, The Johns Hopkins University School of Medicine
- Identified receptors for neurotransmitters and drugs and elucidated the actions of psychotropic agents
- Pioneered the labeling and identification of opiate receptors and used this technique to identify all the major neurotransmitter receptors in the brain
- Co-founded Nova Pharmaceuticals and Guilford Pharmaceuticals
- Holds 41 patents
Baiju R. Shah, Chief Executive Officer of BioMotiv, considers Cleveland a “medical capital,” an undisputed leader in clinical care, medical research and medical device development.

Through BioMotiv’s alignment with the Harrington Discovery Institute, he hopes to broaden the city’s reputation as a national center of innovation to include the developing of new medicines. Industry experts have called the Harrington Discovery Institute the “bridge across the valley of death” in the process of translating scientific discoveries into patient-benefiting products. Now, all eyes are on Cleveland to gauge how well the Harrington Discovery Institute delivers on its mission to overcome the barriers to the process that have reduced the flow of breakthrough medicines to a trickle.

Insider Experience

At the center of the mission are the Harrington Discovery Institute Scholar-Innovators. One of BioMotiv’s purposes is to provide the Harrington Scholar-Innovators with the tangible and intangible means to advance their discoveries closer to commercialization. Among the wealth of resources available to them is the BioMotiv Advisory Board. Comprised of individuals with vast experience in pharmaceutical development, entrepreneurial ventures and development collaborations, the Advisory Board provides guidance on which of the Scholar-Innovator projects show the most promise for further development by BioMotiv.

“These advisors are very interested in this initiative because it addresses a fundamental industry and societal need,” Shah says. “All of these individuals have dedicated their careers to bringing new medicines forward for patients – with a total of 50 marketed products among them – and they are deeply concerned about the breakdown of traditional models,” he explains. “They are impressed by the novelty of our approach and the promise it holds to address the most pressing problem that impedes patients from benefiting from the research discoveries being made at our nation’s research institutions.”

“The talent that the Harrington Discovery Institute and BioMotiv have attracted is unprecedented for early-stage drug development.”
Filling the Void

BioMotiv is focused on identifying and advancing products that are typically too early in development for them to attract financial investment from pharmaceutical companies or venture investors. “By assisting these projects with funding, industry expertise and networking at an early stage, we complete the bridge between the research institutions and pharmaceutical companies, bringing forward new products for patients,” Shah explains.

BioMotiv is one of only a handful of drug development companies that are dedicated to this technology-centric model of drug development. BioMotiv’s link to the Harrington Discovery Institute as an accelerator for groundbreaking new products has captured the attention of disease foundations, pharmaceutical companies, research institutes and policymakers interested in human health and medicine, Shah says.

“The talent that the Harrington Discovery Institute and BioMotiv have attracted is unprecedented for early-stage drug development,” he notes. “The importance of the mission, and the model’s uniqueness and national reach, draw on the experience and capabilities of those who have passion and commitment toward accelerating breakthrough discoveries into medicines.“

Comprised of top-tier experts in early-stage drug development, the BioMotiv Advisory Board is tasked with shaping the company’s portfolio selection strategy, mentoring the Harrington Discovery Institute physician-scientists and sourcing and structuring novel collaboration opportunities. Members of the Advisory Board are established leaders in the pharmaceutical industry who have melded innovation with business acumen to create success. Their expertise ranges from polymer science to genomics to regenerative medicine with a focus on developing successful partnerships and structuring financing to commercialize clinically promising products.

For the Harrington Discovery Institute physician-scientists, the BioMotiv Advisory Board offers an unparalleled opportunity to connect with business and financial experts who know how to translate laboratory research into game-changing therapeutics.

**THE BIOMOTIV ADVISORY BOARD:**

David C. U’Prichard, PhD, chairman, BioMotiv Advisory Board; director, Iroko Pharmaceuticals, LLC; director, Naurex, Inc.; partner, Druid BioVentures

Ronald M. Cresswell, PhD, former CSO of Warner-Lambert and Head, Global Research at Parke-Davis

Christine M. Deboueck, PhD, former SVP of Genomics and Proteomics Research for GSK, Gates Foundation Advisory Board

Frank L. Douglas, MD, PhD, former CSO of Aventis and Chief Science Advisor for Bayer

Diane Jorkasky, MD, former VP, Global Clinical Research for Pfizer and CMO, Endo Pharmaceuticals

Michael L. Nochomovitz, MD, President, University Hospitals Physician Services

Lawrence Olanoff, MD, PhD, former President/COO of Forest Pharmaceuticals

Perry B. Molinoff, MD, former Vice Provost of Research at University of Pennsylvania and VP, Research at Bristol Myers Squibb

Srinivas G. Rao, MD, PhD, former CEO of Kyalin Biosciences and former CSO of Cypress Biosciences

Jonathan S. Stamler, MD, Director, Harrington Discovery Institute

Harlan Weisman, MD, former CSO of Johnson & Johnson Diagnostics & Devices and Chair, R&D, Johnson & Johnson Pharmaceuticals
The **Harrington Discovery Institute Scientific Symposium** brings together the Harrington Discovery Institute at University Hospitals Case Medical Center leadership and Scientific Advisory Board, the Harrington Family, the Harrington Discovery Institute Scholar-Innovator grantees, the Harrington Distinguished Scholars Program early career awardee, the Innovation Support Center team and panel of advisors, BioMotiv leadership and Advisory Board and invitees to celebrate the spirit of discovery that unites these leaders in science, medicine and academia.

With the inaugural meeting in 2013, the Scientific Symposium has assumed its rightful place in University Hospitals Case Medical Center’s nearly 150-year tradition of uniting research and medicine to develop clinical breakthroughs that alleviate human suffering and cure diseases. University Hospitals Case Medical Center first aligned itself with Case Western Reserve University School of Medicine in 1895. Today, the School of Medicine is among the leading recipients of National Institutes of Health (NIH) awards and ranks in the top 25 among U.S. research-oriented medical schools as designated by U.S.News & World Report.

This legacy of discovery and dedication to transforming patient care through innovative scientific research establishes University Hospitals Case Medical Center as a fitting meeting place for the distinguished physician-scientists gathered here for the first Harrington Discovery Institute Scientific Symposium **May 9 and 10, 2013**.

The symposium opened on May 9 with an inaugural lecture by **Solomon H. Snyder, MD, DSc, DPhil**, Distinguished Service Professor of Neuroscience, Pharmacology and Psychiatry, The Johns Hopkins University. The opening presentations included remarks by Harrington Scientific Advisory Board member **Charles L. Sawyer, MD**, Chairman, Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center. Special presenters on Friday included **Margaret A. Anderson**, Executive Director, FasterCures, and **Andrew R. Marks, MD**, Chairman, Department of Physiology and Cellular Biophysics, Columbia University Medical Center, who delivered the keynote address.

For more information about the Scientific Symposium visit HarringtonDiscovery.org.
The Harrington family of Hudson, Ohio, became the most generous philanthropic family in the history of University Hospitals on February 28, 2012. With their gift of $50 million to create the innovative Harrington Discovery Institute, the Harringtons’ total giving surpassed $72.6 million.

The Harrington Discovery Institute is a key part of a pioneering, Cleveland-based national initiative to accelerate the transformation of physician-scientists’ medical breakthroughs into life-enhancing and lifesaving new drugs. The institute aligns with a mission-driven for-profit enterprise to form a powerful system for drug development. The Harrington Discovery Institute addresses a major challenge in medicine today: a lack of resources and commitment to new drug development that has created a wide gap, known as the “Valley of Death,” in which promising research stalls. The result has been a serious decline in approved new medicines.

“We are very excited to support what we see as a national model that will bring new drugs to the market to help patients with heart disease, cancer and other health issues,” says Ron Harrington, who along with his wife, Nancy; daughter Jill; and son and daughter-in-law, Ron and Lydia, made these generous gifts to UH. “Our family became humbled students of heart disease after I was diagnosed. During the process, we marveled at how physician-scientists play a pivotal role in advancing discovery, yet face so many obstacles throughout the process.”