



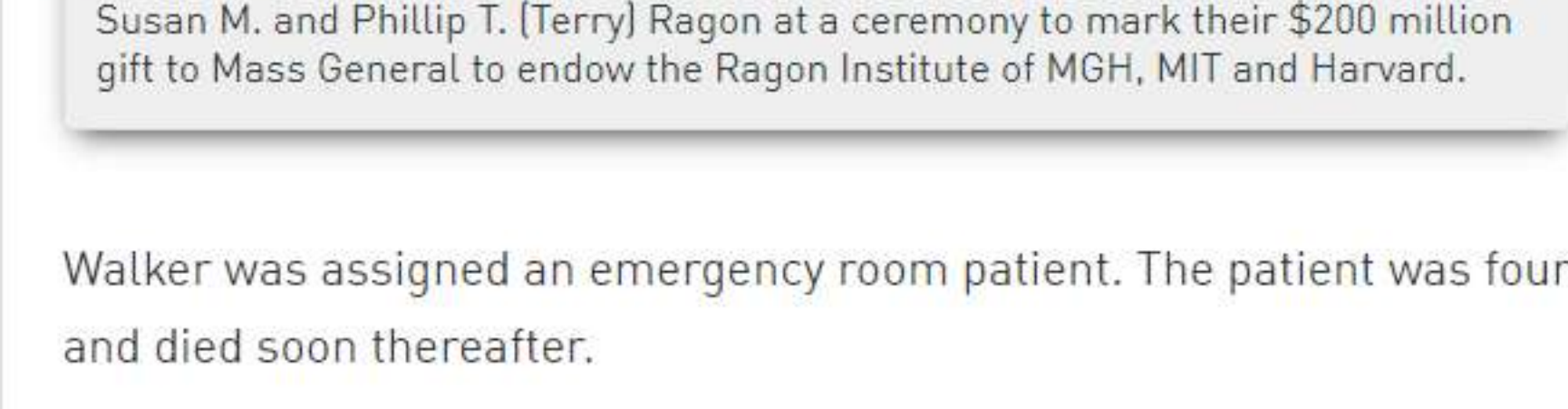
Pictured at the Ragon Institute are, from the left, Bruce D. Walker, MD, its director and Facundo Batista, PhD, its associate director and chief scientific officer.

Ragon Institute: Harnessing the Power of Human Immunity

As the Ragon Institute enters its second decade, a transformative gift from philanthropists Phillip T. and Susan M. Ragon adds fresh momentum to its remarkable fight against HIV/AIDS and other infectious diseases.

Published 8 months ago by Dan O'Sullivan in Donor Recognition, Mass General Magazine, Medical Research

For the Phillip T. and Susan M. Ragon Institute of MGH, MIT and Harvard, a recent \$200 million gift from its namesake donors promises to sustain and create enormous opportunities for research, collaboration and discovery for decades to come.



Susan M. and Phillip T. (Terry) Ragon at a ceremony to mark their \$200 million gift to Mass General to endow the Ragon Institute of MGH, MIT and Harvard.

The Ragon's latest donation — given to Massachusetts General Hospital and jointly governed by the presidents of MGH, MIT and Harvard — is the largest in the hospital's history and will strengthen the decade-old institute's commitment to harnessing the power of the immune system to uncover new ways of preventing and curing human disease. These efforts will continue to be infused with the sense of urgency and determination that its director, Bruce D. Walker, MD, first felt as a medical intern at Mass General.

Walker was assigned an emergency room patient. The patient was found to have multiple infections and cancers and died soon thereafter.

Shortly after his arrival in 1980, Dr.

None of the doctors had ever seen such a case. A few weeks later, another patient presented with similar symptoms and also passed away quickly. As it turned out, these cases heralded the arrival of the AIDS epidemic, the result of infection with the human immunodeficiency virus (HIV).

"It was terrifying," Dr. Walker recalls. "These were young people who came in with a conglomeration of life-threatening conditions and died horrible deaths. All we could do was offer comfort measures."

Dr. Walker became an infectious disease specialist, with a focus on HIV research both at Mass General and at the epicenter of the HIV/AIDS epidemic in South Africa. During one of his trips to South Africa, he was asked to meet Phillip (Terry) Ragon, whose database software company, Intersystems Corp., had installed the electronic medical record system being used at the mission hospital where Dr. Walker's team was working.

"The Ragon Institute is a hub where brilliant minds come together to collaborate and solve intractable health problems."

That meeting led to a 2007 trip to South Africa with Dr. Walker, where Mr. Ragon saw the epidemic's devastation firsthand. He and his wife, Susan, took an interest in Dr. Walker's work and in the vision of bringing together experts from diverse disciplines to harness the immune system to address diseases of global importance and advance the field of immunology. The Ragon's subsequently committed \$100 million to establish the Ragon Institute in 2009, creating a joint venture involving Mass General, MIT and Harvard with the initial goal of developing an effective HIV vaccine.

Expanding Knowledge, Encouraging Progress

The institute's many and varied accomplishments in its first decade inspired the Ragon's to increase their support in a meaningful and long-lasting way.



At the Ragon Institute, scientists from a wide range of disciplines collaborate to address challenging health problems of global importance.

"It is an honor and a great privilege to have the opportunity to participate in such an exciting effort to profoundly affect the lives of many people who struggle with infectious diseases such as HIV," Mr. Ragon says. "We are confident and excited that we are well along the path to a vaccine and, hopefully, a cure as well for HIV and ultimately a broad range of other diseases."

achievements resulting from the interdisciplinary teamwork that is a hallmark of the Ragon Institute," she says. "Our organization was started with the support of some of the greatest local institutions in Massachusetts — MGH, Harvard and MIT. While this is a global effort, its local implications for patients, and their friends and families, are profound."

Mrs. Ragon, vice president of finance, administration and recruitment at InterSystems, also expressed pride in the work of the past decade and optimism for the future. "After a decade of steady progress, we could not be more proud of the success and

Calling the Ragon's "true visionaries," Peter L. Slavin, MD, Mass General president, applauds their unwavering commitment to making the world a better, safer and healthier place. "The Ragon Institute is a hub where brilliant minds come together to collaborate and solve intractable health problems," he says. "Terry and Susan Ragon are two of these enlightened thinkers who through their generosity and vision are saving lives. Their support, leadership, passion and confidence enable the Ragon Institute to think boldly, be daring and aim high now and long into the future."

not be more proud of the success and

Taking a Different Approach

"Cross-disciplinary collaboration and focus on collective unifying goals of global impact are our strengths."

Years ago, Dr. Walker recognized that the typical academic approach to solving complex scientific problems, in which scientists or clinicians work independently, was too limiting. Achieving a goal as ambitious as an HIV/AIDS vaccine, for example, would require a collaborative, interdisciplinary approach.

The Ragon Institute thus fosters partnerships among professionals with different yet complementary backgrounds. They include basic immunologists, clinicians, engineers, computational biologists, physical scientists and geneticists. Together, they focus on collective goals of global importance, learning from patients along the way. These experts span science and engineering disciplines at MIT and Harvard as well as research and clinical care at Mass General.

"I joined the Ragon Institute 3 years ago because I recognized the power of this approach and the need to focus on patients," explains Facundo Batista, PhD, associate director and chief scientific officer. "As a very basic immunologist who had never worked on HIV, I have been able to apply my knowledge not only to HIV but to new Ragon efforts including malaria, Zika virus, influenza, tuberculosis and more.



Ragon Institute research technician Alice Linder and Doug Kwon, MD, PhD, examine a microscope slide that holds tissue from an HIV infected donor.

"We're a human immunology institute," he adds. "It's important that we don't focus solely on HIV. Cross-disciplinary collaboration and focus on collective unifying goals of global impact are our strengths."

in part because the virus makes lots of mistakes as it reproduces," Dr. Walker says. "So even in a given individual, you don't just have one virus. You have all these different viruses with slight mutations in them. That impacts the ability of the immune system to see the infection."

A Problem of Unprecedented Magnitude

Before the Ragon Institute was formed, co-founder Dan Barouch, MD, PhD, had begun work on an HIV/AIDS vaccine. The institute funded early clinical trials of the vaccine in people. Along with the National Institutes of Health (NIH) and the Bill & Melinda Gates Foundation, the institute is now funding studies involving 2,600 women in Africa. Dr. Walker expects Ragon investigators will determine the vaccine's effectiveness within three years.

The World Health Organization (WHO) estimates that 37 million people were living with HIV in 2017. Residents of the WHO African Region represented nearly two-thirds of that figure. Developing an effective HIV/AIDS vaccine — the best hope for ending the epidemic — has proven to be incredibly elusive.

Ragon Institute investigators are also leveraging the same vaccine platform in an attempt to develop a Zika vaccine. "Our goal is not only to make vaccines against these diseases but also to understand how the diseases work so we can make vaccines against other pathogens as well," Dr. Walker notes.

"It's a problem of unprecedented magnitude, in part because the virus makes lots of mistakes as it reproduces," Dr. Walker says. "So even in a given individual, you don't just have one virus. You have all these different viruses with slight mutations in them. That impacts the ability of the immune system to see the infection."

Spontaneous HIV Control

Dr. Walker's laboratory has also been studying people who control HIV infection spontaneously without medications.

Ragon Institute investigators have also been studying people who control HIV infection spontaneously without medications (known as "elite controllers"). In 2010, the lab published a paper showing that a group of related proteins known as the human leukocyte antigen (HLA) dramatically affects whether or not people can control HIV infection on their own.

Through a collaboration with the Broad Institute of MIT and Harvard and more than 300 physicians nationwide, Ragon Institute investigators are examining this phenomenon more closely. More than 1,000 elite controllers have been recruited. Investigators are comparing the amino acids found in the HLA of elite controllers with those of about 2,000 people with progressive HIV infection.

The investigators have found that the immune system in elite controllers creates a trap for HIV: The virus typically mutates to escape detection by the body's immune response. In elite controllers, these mutations cause the virus to no longer function. If the virus does not mutate, though, then it is targeted by the immune system. Either way, the virus fails.



At the Ragon Institute, Abigail Schiff (left) and Elizabeth Byrne, both MD-PhD candidates, discuss a lab image of macrophage cultures infected with HIV. Macrophages are immune cells that specialize in detecting and destroying foreign invaders in the body.

"We've been trying to make an HIV vaccine to prevent infection," Dr. Walker says. "But now we see that we may be able to get people who are already infected to control the virus without medication by changing their immune response to the virus. The best-case scenario would be getting the 37 million people with HIV to control the virus with their own immune systems."

the immune response in mucosal tissues, such as the membranes lining the gut, lungs and female genital tract.

Collaboration Toward Solutions

Dr. Kwon notes that, in most new HIV infections, these mucosal tissues are where HIV is transmitted and establishes infection. To devise new strategies to halt transmission in women, he has explored how the community of bacteria living in the vagina (the vaginal microbiome) affects HIV risk.

Doug Kwon, MD, PhD, has been with the Ragon Institute since its inception and now serves as director of clinical operations. His lab focuses on understanding how HIV affects

Established by Dr. Kwon, Dr. Walker and other Ragon investigators in 2012, the Females Rising through Education, Support and Health (FRESH) program is based in the Umlazi township of South Africa, a country ravaged by the epidemic. The study follows young women who are at risk of acquiring HIV, while simultaneously offering intensive HIV-prevention education and skills training to pull participants out of poverty, one of the main drivers of HIV infection risk. Even with this curriculum and provision of pre-exposure prophylaxis, infections occur with an annual incidence exceeding 8 percent.

Dr. Kwon's group has demonstrated that the vaginal microbiome in healthy African women in FRESH is quite different from that in healthy American women — and is associated with much higher rates of HIV acquisition. They are trying to figure out why so they can translate this understanding into better prevention methods, including a vaccine.

"You have this unique mixture of people with very different scientific backgrounds working together toward a common goal ..."

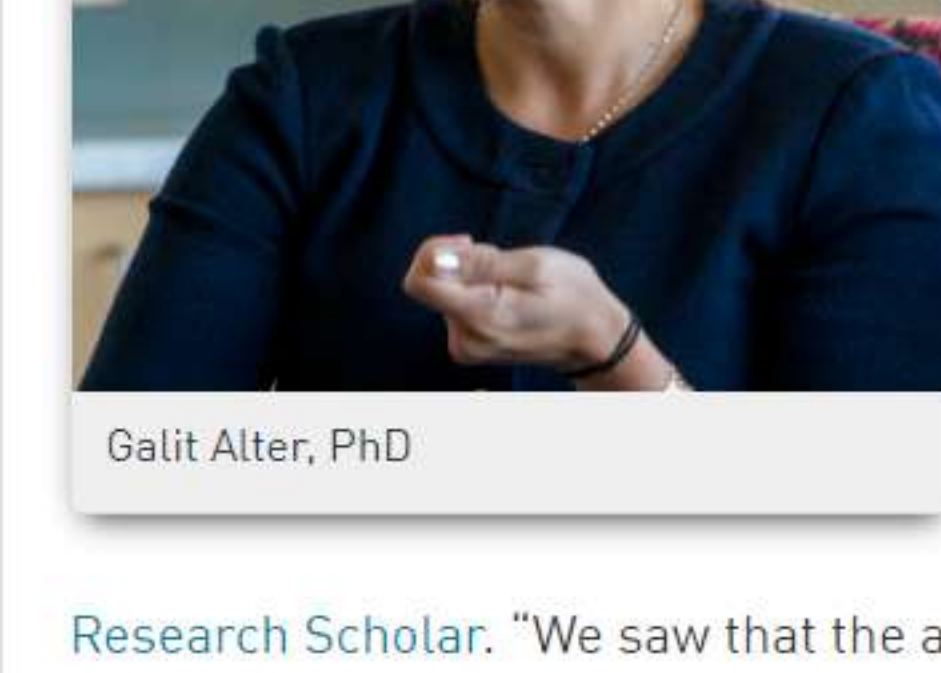
Dr. Kwon, who also sees patients at the Mass General infectious diseases practice, appreciates the Ragon Institute environment. "You have this unique mixture of people with very different scientific backgrounds working together toward a common goal: to apply basic science to impact human disease," he says. "Various areas of science are often siloed with limited interdisciplinary interaction. But the Ragon Institute cuts across these silos to create collaborations to find solutions."

One Medical Student's Inspiration

Elizabeth Byrne spent the summer of 2011 at the Ragon Institute after her freshman year at Harvard. She has since made multiple trips to the FRESH site in South Africa and is now an MD-PhD candidate at Harvard Medical School.

Seeing other young women dealing with HIV has reinforced her commitment to understanding the virus and preventing its transmission.

"My time at the Ragon Institute has shown me how powerful it can be to combine a real understanding of a clinical problem with cutting-edge basic science research," Ms. Byrne says. "We're constantly trying to bring clinical insights back to the lab to inspire new ways of thinking about pathogenesis of disease and of diagnosing, preventing and curing disease. I have been so inspired by the people at the Ragon Institute, who exemplify that cross-disciplinary approach and are bound together by a shared passion for making a clinical difference."



Galit Alter, PhD

The Tuberculosis Priority

People with untreated HIV infection are particularly susceptible to opportunistic infections such as tuberculosis (TB). The WHO says TB is "the number one cause of death among people with HIV in Africa, and a leading cause of death in this population worldwide." The Ragon Institute has thus made studying TB a high priority. In fact, the institute features a facility that allows researchers to safely conduct experiments involving TB and other dangerous pathogens.

Research Scholar. "We saw that the antibodies are very different in people who are controlling TB versus those who are not."

Galit Alter, PhD, is at the forefront of this TB work. Previously, she focused on profiling the role of antibodies (protective proteins produced by the immune system) in HIV. Then Sarah Fortune, MD, director of the Ragon tuberculosis program, gave her lab \$50,000 to profile antibodies in TB. "The data were striking," says Dr. Alter, the Samana Cay MGH

A 2015 study provided evidence that antibodies may help control infection with the bacteria that cause TB. The findings sparked progress in the development of better diagnostic tools for distinguishing between active and latent TB disease along with a more effective vaccine. Dr. Alter is one of the Ragon Institute investigators who will benefit from a sizable NIH grant designated for the development of a TB vaccine.

"For me, there's no place else like the Ragon Institute," Dr. Alter says. "The collaborations, facilities, resources, access to samples, linkages to Mass General and the universities — all of those pieces make it so special."

The Perfect Donors

With the continued flexible, catalytic support from the Ragon's and other donors, Dr. Walker is confident the institute's best days lie ahead.

Reflecting on the past 10 years, Dr. Walker is pleased that the Ragon Institute has been able to unite scientists from diverse disciplines to work critical human health issues. Looking ahead to the next decade, he anticipates the institute will remain a premier center for human immunology while studying the immune system much more broadly in the context of other conditions, such as neurologic diseases and cancer.

With the continued flexible, catalytic support from the Ragon's and other donors, Dr. Walker is confident the institute's best days lie ahead. "Like so many of our donors, Terry and Susan have truly been partners in this," he says. "They're interested in the science and in the work we're doing here and in South Africa. They've struck the right balance between providing their input on strategic decisions and still leaving us with complete independence. They are the perfect donors."

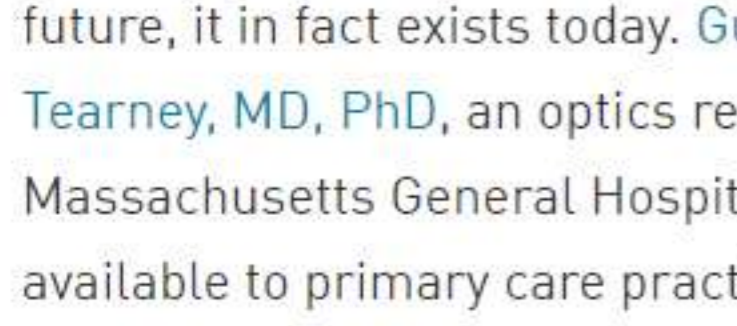
To learn more about how you can support the Ragon Institute of MGH, MIT and Harvard, please contact us.



From left, postdoctoral fellow David Druys, MD, PhD, primary investigator Guillermo (Gary) Tearney MD, PhD, and research design engineer Hamid Farrokh, PhD, access a new imaging prototype device.

Research Scholars: The Power of Bold Giving and Big Ideas

One researcher's development of a swallowable, diagnostic capsule underscores the progress and promise of the MGH Research Scholars program.



Published 2 years ago by Dan O'Sullivan in Donor Recognition, Mass General Magazine, Medical Research

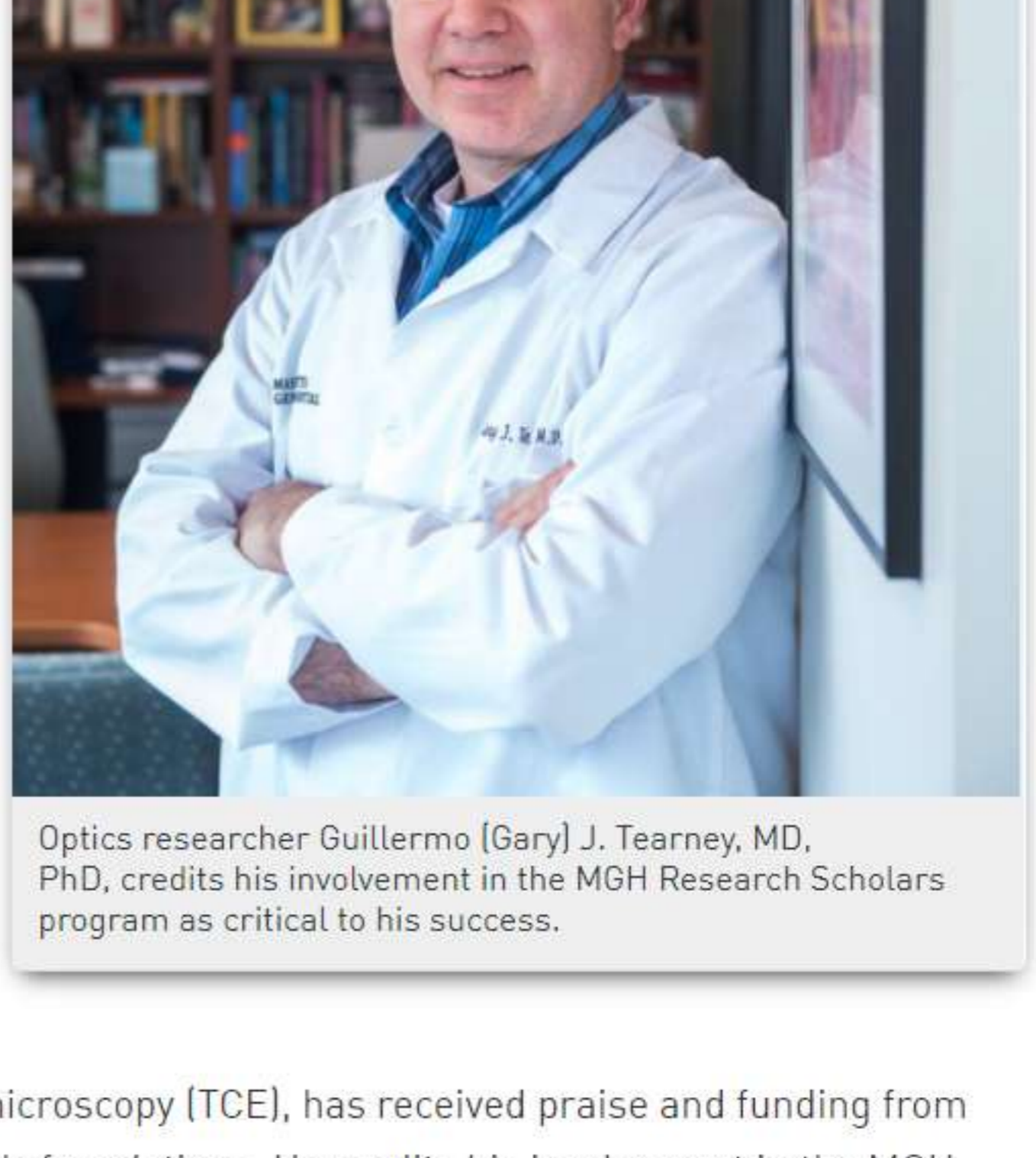
What sort of difference is the MGH Research Scholars program making?

Imagine swallowing a small capsule that travels down your gastrointestinal (GI) tract, capturing multiple microscopic images along the way in order to detect Barrett's esophagus, a precursor to esophageal cancer.

While this device may sound like something from the future, it in fact exists today. Guillermo (Gary) J. Tearney, MD, PhD, an optics researcher at Massachusetts General Hospital, is working to make it available to primary care practices around the world.

Dr. Tearney has long had an interest in GI cancers. Despite the relative ease with which the GI tract can be accessed via the mouth, these cancers still account for more than their share of what Dr. Tearney calls "unnecessary deaths." For example, about 80 percent of people diagnosed with esophageal cancer die within five years.

The traditional approach for diagnosing disease — pathology — can be inefficient, says Dr. Tearney, who was trained as a pathologist. (Pathology involves the study of the causes and effects of diseases, often through laboratory examination of tissue samples.) Dr. Tearney cites the imprecise nature of choosing which part of the organ to biopsy, the risks that come with removing tissue from the body and the extended length of time it takes to make the diagnosis.



Optics researcher Guillermo (Gary) J. Tearney, MD, PhD, credits his involvement in the MGH Research Scholars program as critical to his success.

Greater Freedom to Pursue Research

Dr. Tearney's solution, known as tethered capsule endomicroscopy (TCE), has received praise and funding from the Bill & Melinda Gates Foundation as well as local family foundations. He credits his involvement in the MGH Research Scholars program as critical to his success.

"The MGH Research Scholars program offers greater freedom," says Dr. Tearney, who was the Mike and Sue Hazard Family MGH Research Scholar from 2012 to 2017. "You can have a crazy idea that nobody believes will work, and you can try it."

"The funding allowed me to generate completely new projects that resulted in preliminary data that ended up getting new grants from the National Institutes of Health (NIH)," he continues. "Those grants wouldn't have happened if I hadn't had the freedom to try those high-risk ideas that the MGH Research Scholars program allowed me to pursue."



The tethered capsule developed by Guillermo (Gary) Tearney, MD, PhD, captures images of the gastrointestinal tract.

Rigorous and Competitive Process

Founded in 2011, the MGH Research Scholars program was designed to give exceptional early- and mid-career investigators like Dr. Tearney the funding they need to make transformative advances in their research. This mission is particularly important in an era when funding from organizations such as the NIH is limited.

Mass General researchers must make it through a very rigorous and competitive hospital-wide selection process to gain acceptance to the MGH Research Scholars program. After selections are made, donors who have committed the amount of a full award — \$500,000 over five years — may choose to have one of the MGH Research Scholars named in their honor. Donors may also make a gift of any amount to the program. All donors are offered opportunities to connect with the individual researchers.

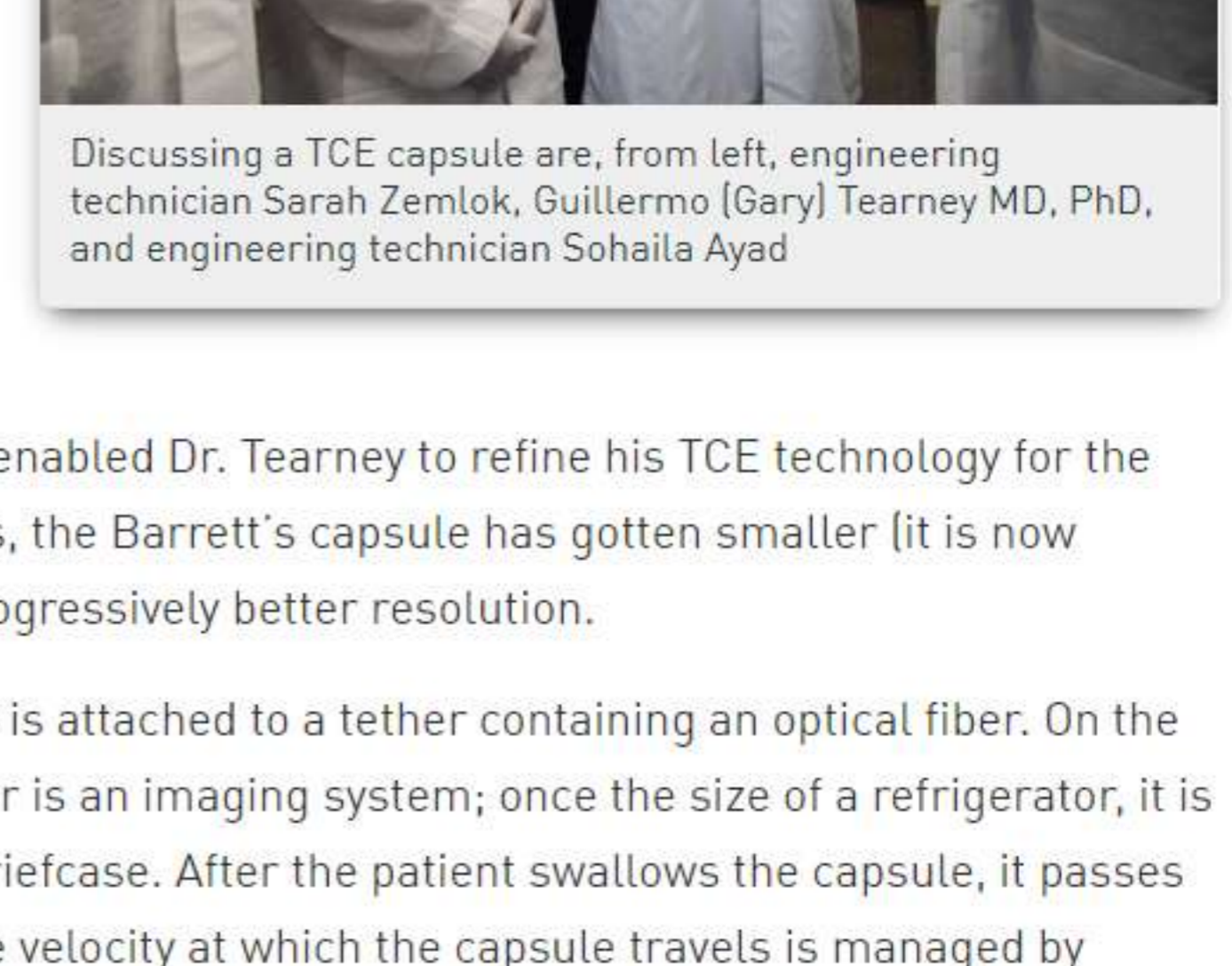
The funding enables MGH Research Scholars to hire more researchers, purchase new equipment and make other essential investments.

Jump-Starting Careers

MGH Research Scholars like Dr. Tearney have also leveraged the money to pursue work that is unlikely to receive initial funding from traditional sources such as the NIH. By generating relevant data from their research, they better position themselves to attract future funding from the NIH or, in Dr. Tearney's case, the Gates Foundation and other organizations. In fact, the first 42 MGH Research Scholars were awarded 277 grants from outside sources totaling over \$292 million.

In addition to the financial benefits, Dr. Tearney values the personal connections that the MGH Research Scholars program has made possible.

"One important factor is the exposure I've gotten to people with tremendous expertise and capabilities — donors, venture capitalists, industry professionals and others throughout various areas of the institution," he says. "All of these things jump-started my career in a way that never would have happened without the program."



Discussing a TCE capsule are, from left, engineering technician Sarah Zemlok, Guillermo (Gary) Tearney MD, PhD, and engineering technician Sohaila Ayad

Refining the Technology

Early in his tenure as an MGH Research Scholar, Dr. Tearney met philanthropists Dorothy and John Remondi at a fundraising event. The couple took a keen interest in his work and went on to become major supporters.

Past support from the Remondi Family Foundation has enabled Dr. Tearney to refine his TCE technology for the Barrett's capsule. Over the course of about 10 iterations, the Barrett's capsule has gotten smaller (it is now roughly the size of a large vitamin pill) while offering progressively better resolution.



Read more about the work of MGH Research Scholars:

- Researcher Studies Diet Impact on Colorectal Cancer
- Trailblazing Engineer Continues Advocacy for Gender Equality in Science
- Heart Attack Prevention Motivates MGH Research Scholar
- MGH Research Scholar Makes Breakthrough in Rare Disease Research

The Barrett's capsule is attached to a tether containing an optical fiber. On the other end of the tether is an imaging system; once the size of a refrigerator, it is now more akin to a briefcase. After the patient swallows the capsule, it passes down the GI tract. The velocity at which the capsule travels is managed by maneuvering the tether.

"While it goes down, the mechanics inside the capsule start spinning and scan a beam around the circumference of the wall of the GI tract," Dr. Tearney explains. "As it does that, light is reflected back from the wall of the GI tract and travels through the optical fiber in the tether. It's received by the imaging system. The system processes the detected light to create a very high-resolution image of the GI tract from where the capsule is at any given point in time."

Work on Primary Care Initiative

The imaging system reconstructs the data being transmitted as three-dimensional microscopic images of the organ being explored. These extraordinarily detailed images give clinicians the information they need to make a diagnosis.

The advantages of TCE technology abound. It provides images of the entire organ — not just a small piece, as is the case with a biopsy. The patient doesn't need to be sedated, which lowers costs and means the process can be completed in an outpatient setting in about five minutes. After the procedure, the capsule can be disinfected and used in other patients multiple times, reducing costs even further. And perhaps most importantly, the clinician can identify the cause of illness — and start the appropriate treatment — sooner.

Currently, Dr. Tearney is working on a primary care initiative for the capsule that has been funded by the Remondi Family Foundation. The generous gift has enabled the Tearney Lab to collaborate with the Department of Medicine to initiate capsule-based screening clinics in selected Mass General primary care centers.

"It's a really exciting development where we're going to use this device in the real world for screening," Dr. Tearney says. "It will be a capability that's only available at Mass General, and we're on pace to start this year."

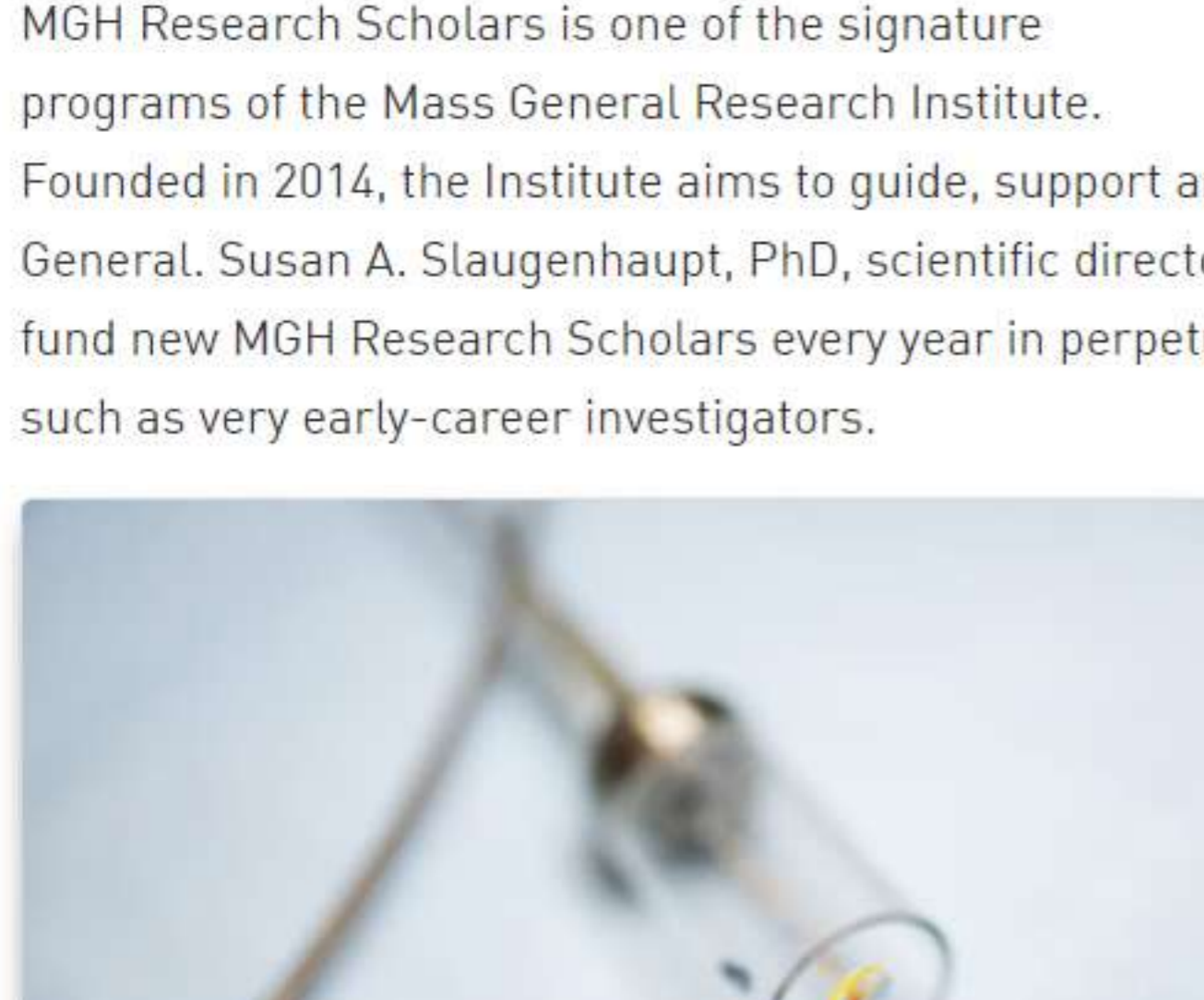


Susan A. Slaughaupt, PhD, scientific director of the Mass General Research Institute, hopes to endow the MGH Research Scholars program.

Funding the Next Great Discovery

MGH Research Scholars is one of the signature programs of the Mass General Research Institute. Founded in 2014, the Institute aims to guide, support and promote the entire research enterprise at Mass General.

In 2014, Susan A. Slaughaupt, PhD, scientific director of the Institute, hopes to endow the program in perpetuity and launch similar programs targeting other subsets, such as very early-career investigators.



A tethered capsule microscopy device during the fabrication process

"Our field is losing young people. They're not pursuing science because it's just too hard," Dr. Slaughaupt says. "It's very difficult to have such insecurity in your life. You want to be able to take home your own paycheck and put dinner on the table for your family, and this insecurity is driving a lot of people away from science."

Dr. Slaughaupt just completed a five-year term as the Elizabeth G. Riley and Dan E. Smith Jr. MGH Research Scholar, an experience she describes as "life-changing." Her research focuses on finding genes and then treatments for a handful of very rare diseases.

Echoing Dr. Tearney's words, Dr. Slaughaupt says she found greater freedom in her research thanks to

the MGH Research Scholars program. "When we write our grants, frequently it's for what I call 'safe science.' In order to get the grant funded in the first place, you have to have a lot of data already suggesting that what you propose will be successful," she says. "With the unrestricted funding that comes from the MGH Research Scholars program, if you want to take a chance — and most major scientific discoveries come from taking a chance — you can do that kind of work."

"It allowed me to pursue some really big experiments to evaluate the effect of the drug we're developing on the entire genome that I wouldn't have been able to do otherwise," Dr. Slaughaupt adds. "That's the kind of impact this program is designed to have. It's about supporting bright, promising investigators who just need the funds to make the next great discovery."

A Valuable Introduction

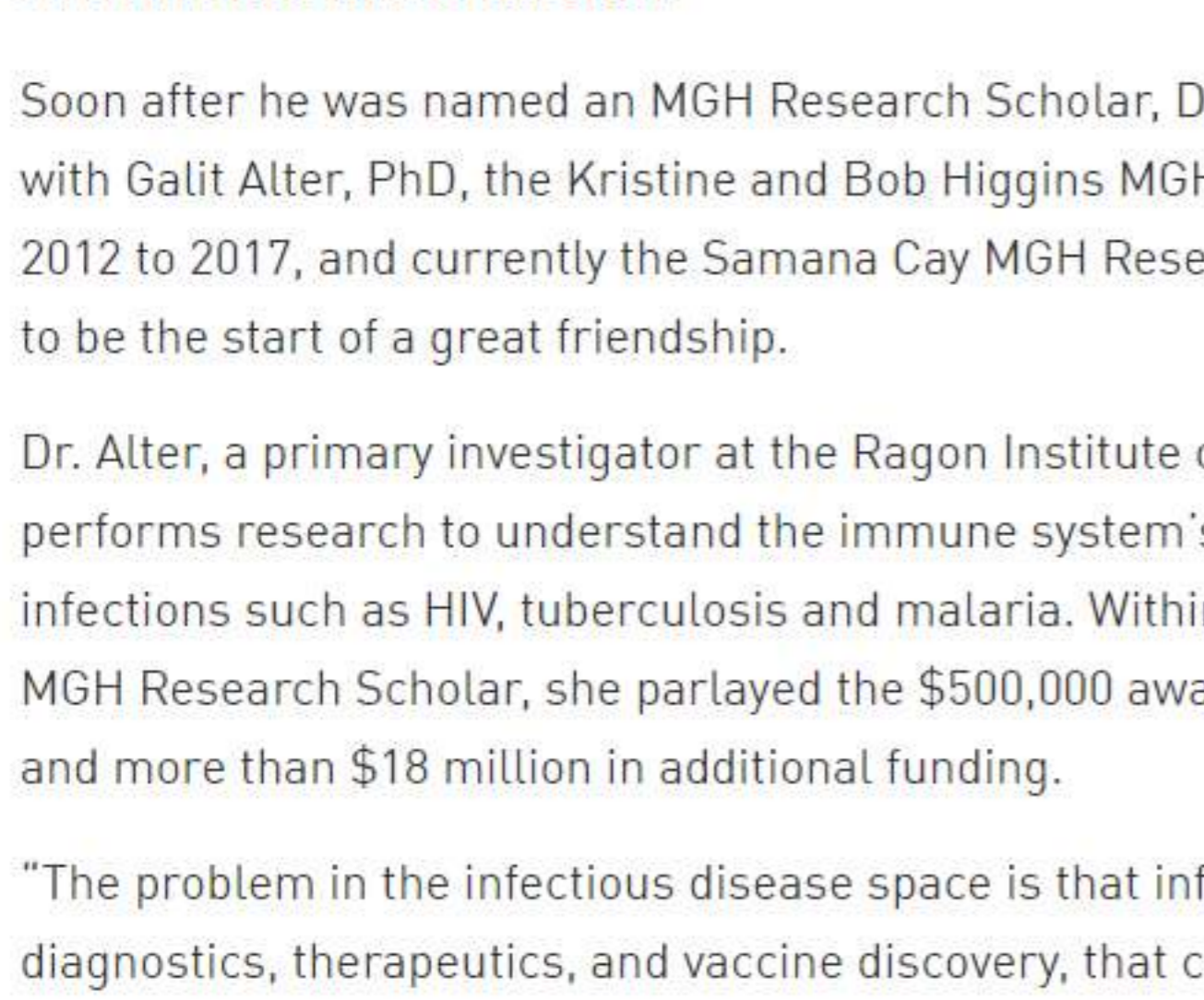
Soon after he was named an MGH Research Scholar, Dr. Tearney crossed paths with Galit Alter, PhD, the Kristine and Bob Higgins MGH Research Scholar from 2012 to 2017, and currently the Samana Cay MGH Research Scholar. It turned out to be the start of a great friendship.

Dr. Alter, a primary investigator at the Ragon Institute of MGH, MIT and Harvard, performs research to understand the immune system's response to chronic infections such as HIV, tuberculosis and malaria. Within a year of becoming an MGH Research Scholar, she parlayed the \$500,000 award into three new patents and more than \$18 million in additional funding.

"The problem in the infectious disease space is that infectious diseases emerge so rapidly, requiring immediate diagnostics, therapeutics, and vaccine discovery, that common funding mechanisms such as the NIH and other funding agencies can't keep up with the required pace of the research," Dr. Alter notes. "The MGH Research Scholars dollars are flexible funds and have been incredibly transformative because I can jump onto a new question the minute I have it."

"That's what the MGH Research Scholars program does," she adds. "It finds these promising minds and allows them to run free. And that's where innovation happens."

"That's what the MGH Research Scholars program does. It finds these promising minds and allows them to run free."



Galit Alter, PhD, (left) parlayed a \$500,000 MGH Research Scholar award into more than \$18 million in additional funding. Also pictured is Mass General researcher Klemen Strle, PhD.

Dr. Alter also appreciates that the program brings together researchers from different disciplines. At the time she and Dr. Tearney met, he was focused on diagnosing early cancer and heart disease. She wondered if his technology could be used to sample immune responses and immune damage deep within tissues. Dr. Tearney has since developed the technology so that it may eventually be able to fulfill the purpose Dr. Alter has in mind as well as other unforeseen applications.

As she got to know Dr. Tearney, Dr. Alter thought the Gates Foundation — which already funded her work — might also take an interest in his research. But first, she encouraged him to emphasize the potential of his technology to enhance understanding of infectious diseases, particularly those of the gut. This was a critical shift. Recognizing that diarrhea is the second

leading cause of death globally among children under the age of 5, the foundation awarded Dr. Tearney a large grant.

"Introducing him to the Gates Foundation and having them start funding his technology and help him push it into the infectious diseases area was huge for Gary," Dr. Alter says. "I want to see him get the support he needs now, at the time that is most critical to building his technology. And then once the technology is there, he can essentially deploy it in a million different ways."

Moving forward, Dr. Tearney will continue to focus on bringing the Barrett's capsule to primary care settings. This work could lead to the development of other primary care-based screening technologies that could catch diseases early and save thousands of lives.

Moving forward, Dr. Tearney will continue to focus on bringing the Barrett's capsule to primary care settings.

As he looks to the future, Dr. Tearney is pleased to be part of Mass General's vibrant research environment. "This is an amazing institution," he says. "It's got top-notch clinical care, a tremendous patient base, many of whom want to participate in research, and a spirit that research is an important component of what we do here. I can't imagine a better place to be."

To learn more about how you can support the MGH Research Scholars program, please contact us.



Under population health management, healthcare providers and insurers agree to a total budget for managing a population of patients.

Population Health Transforms Care Delivery

A pioneer in the field of population health management, Mass General is finding new ways to enhance healthcare quality while also reducing costs.

11 15

Published 2 years ago by Dan O'Sullivan in Health Policy, Mass General Magazine, Patient Care

To get a sense of how a phenomenon called "population health management" is transforming care delivery at Massachusetts General Hospital, consider a recent emergency involving Elizabeth Bennett of East Boston.

On Sept. 13, 2017, the 88-year-old had difficulty breathing. Mass General emergency room doctors diagnosed a flare-up of her congestive heart failure. After a similar episode a few months earlier, Ms. Bennett had been hospitalized for several days.

This time, she was able to choose a different option: acute-level care in the comfort of her home via the Mass General Home Hospital Program. The program is one example of Mass General's leadership in the shift to population health management.

Population health encompasses a variety of coordinated activities aimed at optimizing the collective health of a defined community of patients while also enhancing quality of care and lowering costs.

The Home Advantage

In Ms. Bennett's case, the hospital essentially came to her. When she and her daughter got home from the emergency room, a Home Hospital team nurse was waiting to assist with the transition. Within 24 hours, Ms. Bennett was visited by a physician, who continued to support her care team, which included a nurse practitioner and a nurse.

For eight days, the care team visited Ms. Bennett twice daily, carefully monitoring her vital signs and checking lab tests. She had round-the-clock access to the team for questions or concerns. Her home care was expanded to include treatment of a chronic obstructive pulmonary disease flare-up. Overall, her health improved steadily.

"To be in your own home, treated so well and have the consistency in the nursing staff was a huge advantage."



Eric M. Weil, MD, chief medical officer for primary care at the Partners HealthCare Center for Population Health, says population health encourages providers to be more proactive.

"I can't say enough about the staff from Mass General," Ms. Bennett's daughter (also named Elizabeth) exclaims. "No one likes being in the hospital. To be in your own home, treated so well and have the consistency in the nursing staff was a huge advantage."

Breaking from Tradition

Population health represents a break from tradition. Historically, insurers have paid healthcare providers on a fee-for-service basis. Critics contend this system incentivizes providers to focus on the quantity of care (i.e. delivering more treatments) rather than the quality.

The population health model features alternative payment systems in which providers and insurers agree to a total budget for managing a population of patients. Providers that stay below the target are rewarded with "shared savings" payments. Providers that exceed the target are penalized.

Eric M. Weil, MD, chief medical officer for primary care at the Partners HealthCare Center for Population Health and a primary care doctor at Mass General, says population health encourages providers to be more proactive.

"Essentially, we're given a population of patients for whom we are responsible. That responsibility transcends the brief time that each patient spends with us during office visits," Dr. Weil explains. "Population health offers strategies to help the clinician deliver all those other components of care that must occur outside the 15-minute slot we get to see the patient in the office."

The Root of the Problem

Timothy G. Ferris, MD, MPH, became CEO of the Massachusetts General Physicians Organization (MGPO) in August 2017. A Mass General internist, he was previously senior vice president for population health management at Partners HealthCare, Mass General and the MGPO.

Dr. Ferris says the industry has long struggled with healthcare costs growing faster than inflation. This reality has wide-ranging implications.

"To the extent that the government is paying for health care — as with Medicare — then as healthcare costs go up, fewer and fewer tax dollars are available for education, the criminal justice system, housing and so on," Dr. Ferris notes. "For employers, it means spending more on healthcare benefits and having less to spend on wages. It also makes American goods and services more expensive than international competitors, and thus less competitive."

Combine these pressures with the aging of "baby boomers" — along with Affordable Care Act-related regulations focused on cost containment — and it's clear reducing healthcare costs is a critical priority for industry and the country as a whole. Can this goal be achieved without sacrificing quality or access to the latest innovations?

Dr. Ferris answers this question in the affirmative. "The good news is that we now have technology like smartphones, electronic health records and the Internet at our disposal," he says. "All of those provide us with new platforms for delivering health care more efficiently."

A Successful Pilot Program

Mass General rolled out its first population health program in 2006, with funding from the federal Centers for Medicare & Medicaid Services (CMS). The three-year pilot program tested strategies to improve the coordination of Medicare services for patients with multiple medical conditions or at least one severe chronic condition.

The program's premise was that providing more tailored, comprehensive care would help keep such medically complex patients healthier and out of the hospital. Indeed, results showed that emergency department visits dropped 13 percent and hospital admissions fell by 20 percent among enrolled patients. Mass General realized annual net savings of 7 percent in caring for these patients and a return on investment of at least \$2.65 for every dollar spent on the program.

In 2009, CMS renewed the project for three years and expanded it to include patients from two other Partners institutions. Today, Partners' Integrated Care Management Program (iCMP) embeds nurse care managers in all of the system's primary care practices to help coordinate care for the 5 percent most medically complex patients, regardless of their insurer.

"The iCMP is now considered the standard of care for this type of patient population," Dr. Weil says. "People from all over the country and the world come here to learn about the system."

Dr. Ferris says about 80 percent of Mass General primary care patients and 15 to 20 percent of specialty patients are now covered under the population health model. (The percentage of specialty patients is so much lower because Mass General serves as a tertiary referral center for other hospitals.)

Better Outcomes Through eConsults

Electronic consultations, or eConsults, are another example of how population health is producing benefits. Suppose a primary care physician (PCP) suspects her patient has a condition that requires a specialist's attention. Traditionally, the PCP would make a referral to a specialist, which might mean the patient waits weeks for an appointment. Then the patient would take time away from his usual daily activities for the office visit.



Timothy G. Ferris, MD, MPH, CEO of the Massachusetts General Physicians Organization, says technology provides new platforms for delivering health care more efficiently.

eConsults, which Mass General introduced in December 2013, streamlines this process. The PCP logs in to the system and makes her request via the patient's electronic health record. The appropriate Partners specialist is paid to respond within 48 hours. As a result, the patient receives effective treatment faster and avoids an unnecessary trip to the doctor.

Mass General projects that about 10,300 eConsults will have been completed at the hospital by the end of 2017. According to Sandhya K. Rao, MD, medical director for specialty programs at the Partners Center for Population Health, medical director for quality assurance at the MGPO and a Mass General internist, the results have been quite positive.

"As a PCP, it used to be that if a patient needed the opinion of another doctor, I would make a referral," Dr. Rao says. "Now, because of population health, we're paying specialists to help PCPs like me take better care of our patients. eConsults represent more of a team-based model, and it's helping us avoid a lot of visits over a patient's lifetime."

Managing Core Tasks

Another way Mass General physicians care for patients outside of office visits is through the use of patient registries. The National Institutes of Health defines a registry as "a collection of information about individuals, usually focused around a specific diagnosis or condition." At Mass General, each PCP is matched with a population health coordinator. That coordinator reviews the PCP's registry and manages the core tasks needed to keep each patient healthy.

"We can specify the types of things to look at, such as medications taken, date of most recent visit and disease stage," Dr. Rao says. Based on that information, the population health coordinator can determine, for example, when a diabetic patient is due for a blood sugar test.

"Keeping registries up to date is something that doesn't need to be done by physicians," Dr. Weil adds. "That frees them up to do the more complex things they were trained to do."

Population Health Transformation

Dr. Ferris is pleased with the progress Mass General has made with population health. There has been ample evidence of cost savings, even with investments the hospital has made in new ways of delivering care.

It's not just about the dollars and cents, though. Daniel M. Horn, MD, associate medical director of the MGPO, estimates that "doing proactive surveillance of our patients with chronic disease and preventive care gaps prevents over 100 cardiovascular events or deaths per year."

Dr. Ferris, meanwhile, points to improvements in hospital admission rates, emergency room visits by medically complex patients, patient satisfaction and other quality measures.

"We have enough experience with population health to know the investments we're making are paying off and we're on the right track," he says. "We haven't solved all the problems we need to by any means, but we have enough demonstrations of truly effective transformation that we're confident it's possible to do this. So we have to keep trying."

"We have enough experience with population health to know the investments we're making are paying off and we're on the right track."

"People from all over the country and the world come here to learn about the system."

"The good news is that we now have technology like smartphones, electronic health records and the Internet at our disposal."