

# INNOVATION

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# First CAR-T Approval Begins New Era in Modern Medicine

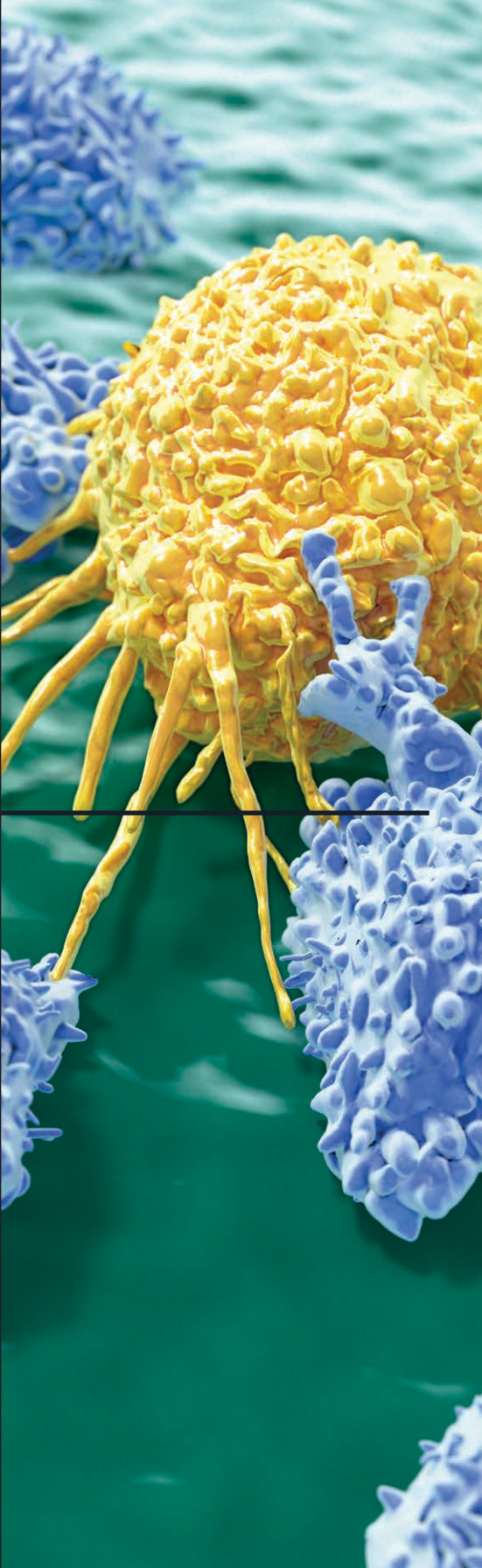
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Specialists in the field of immunotherapy were strongly encouraged by the FDA's approval of the first CAR-T therapy for cancer patients last month.

"This is an exciting time for patients, for the scientific fields of gene and cell therapies, and for cancer in general," says Marcela Maus, MD, PhD, Director of Cellular Immunotherapy at the Mass General Cancer Center. "It's not every day that an entirely new platform of treatment comes along, especially one that is so potent and offers the chance of durable remission."

The recently approved therapy, called Kymriah, was developed by Novartis for pediatric and young adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). ALL is a blood-based, or liquid cancer, that results in the overproduction of cancerous immature white blood cells. It is the most common type of cancer in children, according to the National Cancer Institute.





The safety and efficacy of Kymriah were demonstrated in a multicenter clinical trial of 63 pediatric and young adult patients with relapsed or refractory B-cell precursor ALL where the overall remission rate was 83 percent.

“It’s really clinical and regulatory validation of a development that has been going on for the better part of 25 years,” says Pat Fortune, PhD, Vice President of Market Sectors for Partners Innovation. “This is the first approval, and its performance based on clinical trial results is quite remarkable.”

Fortune noted that more CAR-T treatments are in the development pipeline and should be heading to the FDA for approval soon. “By last count, conservatively, there are 40 individual CAR-T therapies in the stage of clinical trials moving to approval, and this is just the beginning of that process.”

“Since the therapy, at least in the way it has been used so far, is so remarkably successful, this is really a seminal event with respect to the outlook for cancer patients—initially for hematological cancers and hopefully for solid tumors, although that has yet to be proven.”

The basic concept behind CAR-T is to take a patient’s own T-cells, which are responsible for directing the body’s immune response to invading agents, and reengineer them in the lab to detect and respond to antigens produced by tumor cells.

One way that cancer cells spread unchecked throughout the body is by mimicking the proteins expressed by “safe” cells in the body, thereby avoiding detection and elimination by the immune system.

Once the T-cells have been reprogrammed to identify and attack a protein expressed by the tumor cells, they are replicated in the lab and injected back into the patient. If all goes according to plan, the T-cells will attack the tumor cells and send the cancer into remission.

Partners HealthCare is contributing to the development of CAR-T and other immunotherapies for cancer, both as a host site for clinical trials at BWH and MGH, and in developing new CAR-T treatments via the Cellular Immunotherapy Program run by Dr. Maus, Fortune said.

Immune-based therapies being tested in clinical trials include CAR-T therapies and first-in-man studies for oncolytic viruses (viruses that have been reengineered to attack and kill cancer cells instead of healthy cells), among others.

In CAR-T therapies specifically, Dr. Maus has an active development program and will be moving some of her discoveries into clinical trials within the next 12 to 18 months.

While the initial results from CAR-T are promising, significant hurdles remain. For one, it has yet to be determined what the long-term outcomes of treatment will be—if and when the blood cancers will recur for patients down the line. Since the therapies are new, it is too early to determine the long-term prognosis.

There is also the challenge of managing cytokine release syndrome, which is a complication of CAR-T treatment where cytokines (proteins that induce an immune response) released by the modified T-cells once they are injected back into the body produce a systemic inflammatory response similar to that of a severe infection.



More work also needs to be done to determine which patients will respond to CAR-T therapies and which will not.

Lastly, there is the question of affordability. The pricing for Kymriah is estimated at \$450,000 for treatment. “One would think that as more therapies come out, the price will come down,” Fortune says. “But these are very expensive therapies to develop; which of them will be affordable in the end still has to be sorted out.”

“Right now, the manufacturing process is complex, labor-intensive and requires expensive reagents that make it difficult to treat large numbers of patients,” adds Maus. “I think improvements in manufacturing or in equipment that allow individual hospitals to manufacture the cells could be revolutionary.”

Finally, while there are clinical trials testing CAR-T therapies on solid tumors in the clinic, solid and liquid tumors don’t look quite alike, and it may be more challenging to produce the same kind of dramatic results, Fortune notes.

While challenges remain, Maus is optimistic that the field will make significant advances over the next few years.

“We are going to see genes introduced with different levels of precision to make CAR-T cells, to make other engineered cells, and that will include the use of gene-editing techniques that make T cells safer, more potent and more widely available, including ‘off-the-shelf’ T cells that don’t have to be personalized for every patient.” ■

# New Stroke Rehab Unit Opens in Malta through Hard Work of PHS Experts

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It's difficult enough to coordinate patient care across departments or hospitals, but what happens when the care process takes place on two different islands?

That was just one of the challenges tackled by an interdisciplinary team from Spaulding Rehabilitation Network (SRN) and Partners HealthCare International (PHI) that recently traveled to the VGH Karin Grech Hospital (KGH) in Malta for the opening of a newly renovated, 28-bed stroke rehabilitation unit.

Part of the Vitals Global Healthcare (VGH) network, the unit's launch is the first step in a comprehensive plan to improve the care for stroke patients and one of a series of initiatives taking place as part of a multiyear agreement between PHI and VGH, explains Betsy Cox, Director of Global Nursing Programs for PHI.

Other initiatives include programs to improve quality and safety, strengthen the program infrastructure, information technology, nursing, and clinical rehabilitation care, Cox says. “We are working on quality and safety with them, moving toward international accreditation, and working closely with nursing leadership development.”

Malta is an archipelago in the Mediterranean Sea that includes the larger island of Malta and the smaller island of Gozo and sparsely populated island of Comino. It is located about 50 miles south of Italy. Approximately 700 patients on the two islands suffer strokes each year. Stroke patients receive care on either island and the goal is to define a stroke pathway across the continuum of care for patients across Gozo and Malta to provide the right level of care at the right time to improve outcomes, satisfaction and efficiency.

“In Malta patients who have suffered a stroke are admitted to Mater Dei Hospital for acute care management. What the patient needs next is dedicated rehabilitation care to start relearning skills,” explained Stephen Zammit, MD, CEO of VGH’s Karin Grech Hospital. “Through our collaboration with Partners and Spaulding Rehabilitation Network we are now able to offer our patients this specialized rehabilitation.”

The new rehabilitation unit at Karin Grech Hospital is located within an existing area of the hospital. The newly opened unit was refurbished to focus exclusively on stroke rehabilitation and features an updated gymnasium and new technologies to assist in the recovery process.



In addition to the facility updates, the teams collaborated on new strategies for educating staff, scheduling patients, conducting case discussions, setting goals for patients, involving families in the care process, and preparing for the next transition of care.

“We’ve delivered some of the work and we will continue to work with KGH remotely as they implement these changes and review targeted performance measures to see how well they are improving care in stroke rehabilitation,” Cox explains.

Cox was quick to highlight the critical role played by the team from SRN, which included physicians, nurses, speech language pathologists, physical therapists, and occupational therapists. “They worked hand in hand, shoulder to shoulder to help our colleagues in Malta through this process.”

PHI, the international arm of Partners HealthCare, has been collaborating with hospitals and health care organizations across the globe for more than two decades. The PHI team merged with Partners Innovation in 2016. The unique model of international collaboration is based on a two-way exchange of ideas rather than exporting a single approach or methodology. In this case, the goal was not for VGH to do everything the same way that the Spaulding team does it, but to combine global best practices with local considerations and identify solutions that work best for this country.





While the advisory teams from Partners have a lot to offer their international colleagues, there is much to gain as well.

“You always learn how our international colleagues do things differently,” Cox says. “Maybe they are using protocols from the European Union or have different cultural practices. You are always extracting ideas from each other and being able to say, ‘Hey, I didn’t think about it that way—we might be able to implement that.’”

For Cox, one of the most gratifying parts of the collaboration is watching the spirit of teamwork develop as the project moves along, not only between the PHI/Spaulding and VGH teams but within VGH as well.

“I think it’s always extremely rewarding to see how these teams that have come from across the globe, and there locally, across two islands, are able to work together and have this impact when so many of them didn’t even know each other beforehand.”

“They come from the same hospital or the same country. Now, not only do they know each other, but they are standardizing care in a way that will have an impact on the patient.” ■

# Center for Clinical Data Science Lays Groundwork for Success in Healthcare AI

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Artificial Intelligence (AI), machine learning, and deep learning are the hottest categories in healthcare right now, but the truth is these concepts have been around for a while, says Trung Do, Vice President of Business Development for Partners Innovation. “The fundamental goal is in extracting meaningful insights from massive amounts of data and making them actionable.”

What’s new is the tremendous amount of computing power that is now available to develop, test, validate, and translate applications (e.g. algorithms and models), at scale, into clinical use, which has the potential to revolutionize the way healthcare is delivered.

Leading the Partners HealthCare AI effort is the new Center for Clinical Data Science (CCDS), a collaborative effort between MGH and BWH that is directed by Mark Michalski, MD, executive director of CCDS.

Founded in 2016, the Center is designed to support Partners’ investigators as they develop AI capabilities and to create and foster a community of like-minded people who are working to advance healthcare through AI and machine learning.

“In the past, if I wanted to find a new way to identify patients with pancreatic disease before they show symptoms, I would come up with a hypothesis and test it in new patients,” explains Keith Dreyer, DO, PhD, Chief Data Science Officer at Partners HealthCare. “But now we’re asking the machine to look into the archives for the answers.”



“I can take millions of past images that show healthy and diseased pancreases and, along with additional medical data on the patients, load them into software algorithms. With that information, the algorithms can learn to recognize those with pancreatic disease, and learn to identify markers that are precursors to their condition. It can then look at current patients’ medical records and pinpoint patients who might develop pancreatic disease and need diagnostic evaluation.”

In one recent project, for example, Dr. Michalski, used hundreds of thousands of medical images to train a computer system to detect strokes, measure tumors and look for traumatic injuries and fractures. The early results are encouraging. “The technology really does work,” he says.

AI’s potential to improve health care delivery is not just limited to imaging, Dreyer notes. “We’re also looking at genetic and genomic data, laboratory data, and other data available inside the electronic medical record and beyond.”

Partners leadership believes AI will play a crucial role in advancing research and improving the delivery of health care in the years to come, Dryer says. “We see this as a new discipline that will be part of every clinical program, every operational program within our system, to improve the way in which we deliver care and the way in which we manage operations.”



The CCDS has initiated a series of strategic relationships that are designed to support these efforts. This includes building computing infrastructure and development capabilities through collaborations with technology companies such as NVIDIA and large international healthcare companies such as General Electric.

“If we do it right, we think there are commercial opportunities for us to take these technologies, learnings and capabilities outside the walls of our system and create real value broadly for clinicians and patients,” Do says.

While the concept of AI and machine learning may not be entirely new, there are good reasons why the field has gained momentum in the past few years, Dryer explains.

One key factor is that the computational power needed to process and draw insights from large data sets is less expensive and more readily available. For many years, the only places that could afford large-scale computational platforms were big companies such as Amazon and Google.

But recently, companies such as NVIDIA have made supercomputers affordable to anyone, and a lot of that is driven by technological advancements in other industries, such as video gaming.

This has enabled Partners HealthCare to acquire a tremendous amount of supercomputing power. The CCDS announced its first agreement with NVIDIA in April of 2016, and over the past year and half it has built one of the most significant supercomputing infrastructures of any academic medical center.

The next step is to combine this computing power with clinical expertise, Dryer says. “You can have really talented data scientists and engineers, but it’s difficult for them to develop health care applications and solutions without a deep understanding of the clinical use case. You need access to clinicians who understand the clinical challenges and who can integrate these applications into the workflow to optimize their effectiveness and adoption by clinicians.”



Another critical element is access to clinical data, which resides within health care systems such as Partners.

“Two years ago, we started to see a lot of companies coming to us and asking for this data,” Do says. “Thanks to the foresight of strategic leaders such as Dr. Dreyer and James Brink, MD, Radiologist in Chief at MGH, who understood the value of our system asset, we decided to make an investment in ourselves to keep the program in-house.”

And that decision is paying off. In May 2017, the CCDS announced a significant 10-year strategic collaboration with General Electric to build a learning factory—a platform with a set of capabilities and tools to support new clinical applications designed to improve patient care.

“The second thing we are doing with the GE relationship is building specific clinical applications, meaning apps that will be sitting on top of this platform or at least integrated into the platform to help clinicians manage and deliver more efficient and optimal care,” Dryer adds.

“Our view of AI is to augment what the clinician is already doing, to make them much more efficient, more accurate, and provide higher-quality discoveries, diagnostics and treatment. For us, it’s about making the clinician better, not obsolete. That’s our strategy.”

Join Us at Partners HealthCare’s 2018 World Medical Innovation Forum, which will focus on the advancements and opportunities of Artificial Intelligence. The Forum will be held on April 23-25, 2018. For more information, [www.worldmedicalinnovation.org](http://www.worldmedicalinnovation.org)





Join Us in

2018

artificial intelligence





The 2018 World Medical Innovation Forum focuses on the advancements and opportunities of Artificial Intelligence. The 2018 event will bring together industry-leading CEOs, Partners' clinical and research experts, investors and deal makers to share perspectives on how cognitive computation, machine learning and big data are having a transformative impact on patient care. International experts will be joined by 1,000 attendees from the senior ranks of the information technology, life science, pharmaceutical, government and health care investment communities, as well as top Partners HealthCare faculty and staff.

**Registration is now open.**

[www.worldmedicalinnovation.org](http://www.worldmedicalinnovation.org)

**April 23–25, 2018**



# Navigating the Innovation Lifecycle: **Bringing New Ideas to Healthcare**

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S E R I E S

The Innovation Symposium Series is a complimentary five-part speaker series focused on navigating the commercial innovation lifecycle. The Symposium Series is open to any PHS-affiliated investigator, clinician and administrator working on, or considering, research that has the potential to be a commercial product. Non-PHS guests are welcome based on available capacity. Each symposium will conclude with a networking reception.

Each Symposium session is richly designed to provide the education, tools and real-world examples needed to help commercialize your research.

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Join us and learn how to pave a pathway to commercialize your research:

- Position your ideas and market them to Industry
  - Manage your intellectual property
  - Negotiate research and material transfer agreements
  - Develop agreements for commercialization of intellectual property
  - Provide guidance and network for start-up opportunities
-

## Introducing the Symposium Series: Attend One, Attend All

### **Filling the Gap: Translating your research via Disease Foundation support**

Translation research funding is the bedrock upon which medical innovation rests. Join us to learn about effective strategies and important issues to consider when seeking translational research funding from disease foundations. Registration is OPEN. **Click here** to secure your seat!

Tuesday, September 19th from 5:00 PM–7:30 PM at the BWH Bornstein Amphitheatre

### **IP Protection: Safeguarding your research for commercialization**

Intellectual property is the cornerstone of commercial licenses. Attendees will learn how protection is obtained, how investigators can help strengthen the protection of their invention, and the impact recent court decisions have on biological inventions.

Tuesday, October 17, 5:00 PM - 7:30 PM, MGH Simches Research Center Auditorium

### **Navigating Healthcare IT: Winning strategies to commercialize your HIT invention**

The opportunities and challenges of commercializing Healthcare Information Technology, or HIT, are different from those in typical patent based licensing. Experts will identify these distinguishing features and provide insights about the direction of future technologies.

Tuesday, December 7, 5:00 PM - 7:30 PM, BWH Bornstein Family Amphitheater



### **Industry Insights: Positioning your research to a Commercial Partner**

Pitching a research program to industry for funding support requires that investigators understand the motivations and needs of companies that sponsor academic research. Learn first-hand from an industry leader how to position your research more effectively to gain interest and funding support. Hear from peers how they mastered the challenges and pitfalls of landing a commercial partner.

Wednesday, January 24, 5:00 PM - 7:30 PM, MGH Simches Research Center Auditorium

### **Case Closed: Taking the mystery out of Start-ups and Venture Capital funding**

Medical innovation often enters the market via start-ups supported by venture capital investors. Attendees will hear first-hand from a well-known investor the criteria used when making investment decisions. A panel of peers will discuss the venture capital finance models they used and the paths chosen to get innovative medical technology to patients.

Wednesday, February 28, 5:00 PM - 7:30 PM, MGH Simches Research Center Auditorium



## Filling The Gap: Translating Your Research Via Disease Foundation Support

The first Symposium Session will convene on Tuesday, September 19th from 5:00 PM – 7:30 PM at the BWH Bornstein Amphitheatre.

This session will provide hands on strategies for obtaining translational research funding from disease-focused foundations. Faculty and employees will gain insight into disease foundations and the many ways they support translational research.

This session will address the following questions:

- What gaps do foundations address?
- What is the impact of foundations?
- How do foundations measure success?
- How do I position my research around their highest priorities?
- How should I prepare when approaching a foundation?

### SESSION SPEAKERS:



**Howard Weiner, MD**  
Director, Multiple Sclerosis Program,  
Brigham and Women's Hospital;  
Robert L. Kroc Professor of Neurology,  
Harvard Medical School



**Guillermo Tearney MD, PhD**  
Mike and Sue Hazard Family MGH  
Research Scholar; Professor of Pathology,  
Harvard Medical School



**Omid Farokhzad, MD**  
Director, Center for Nanomedicine,  
Brigham and Women's Hospital;  
Professor of Anaesthesia,  
Harvard Medical School



**Walter Kostich, PhD**  
Director, Commercial Research,  
National Multiple Sclerosis Society

### SESSION AGENDA:

5:00 PM – 5:30 PM	Registration
5:30 PM – 5:45 PM	Principal Investigator Experience
5:45 PM – 6:25 PM	Fireside Chat
6:25 PM – 6:55 PM	Panel Discussion
6:55 PM – 7:00 PM	Summary / Wrap-up
7:00 PM – 7:30 PM	Networking Reception

Visit [innovation.partners.org/innovation-symposium-series](https://innovation.partners.org/innovation-symposium-series) for more information.

Don't miss out on this informative session. **Register today!**

**REGISTER NOW**



INNOVATION DISCOVERY  
GRANTS PROGRAM

# IDG Supports Healthcare AI Applications

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If you have an idea for improving healthcare in the field of artificial intelligence (AI), data science, cognitive computation, or machine learning that has the potential to turn into a commercial project, the organizers of the Innovation Discovery Grants Program (IDG) want to hear from you.

Now in its third year, the IDG awards will provide funding for proof-of-concept and validation studies for ideas that have the potential for commercialization. A total of 10 projects will be funded in 2018 for up to \$50,000 each, inclusive of 15 percent indirect costs.

Pre-proposals are due on September 25th and will be evaluated on a variety of factors, including the potential healthcare impact of the idea, the probability of meeting milestones during the award period, the likelihood that achieving the endpoints would lead to further development (either by creating a spinoff company or partnering with industry), and the potential for attracting further investment.

## Innovation Discovery Grant Winners Detail the Benefits of the Program

Previous recipients of Innovation Discovery Grant (IDG) awards say the program not only helped them move projects from their lab closer to the clinic, it also helped them build valuable connections to members of the biotech, venture capital and commercialization fields.

Howard Weiner, MD, the co-director of the Ann Romney Center for Neurologic Diseases at Brigham and Women's Hospital, received a 2016 IDG grant to support an innovative new approach to immuno-oncology that was developed based on insights his laboratory team had while developing strategies to fight multiple sclerosis.

In 2016, a new company, Tilos Therapeutics, was launched as a spinoff of the Partners Innovation Fund to continue developing new therapies for cancer patients based on the approach developed by Dr. Weiner and his team.

"Because of the IDG program, we were able to prepare our findings for translation to the clinic," Weiner says. "I would strongly recommend any investigator wanting to develop an innovative finding they have to apply for an IDG grant."

Lynn Bry, MD, PhD, Director of the Massachusetts Host Microbiome Center in the Department of Pathology at BWH, also received an IDG award in 2016, which she used to fund confirmatory research on the use of therapeutic microbes for the treatment of food allergies.

Bry and her team are developing beneficial bacteria that could help to prevent food allergies from developing in infants, and stop allergic reactions in adults. They have formed a company, Consortia Therapeutics, to bring their therapies to market.



## INNOVATION DISCOVERY GRANT WINNERS DETAIL THE BENEFITS OF THE PROGRAM (CONT.)

The IDG program also gave Bry a platform to promote the team's work to investors and potential collaborators, including the Partners Innovation Board of Advisors, the Partners Healthcare Board of Trustees, and the BWH Board of Overseers. It also helped her to pursue other sources of funding.

"There are a wealth of resources in Massachusetts alone that can help get new ideas to commercial application," she says. "Per my role as Director of the Massachusetts Host-Microbiome Center, we received a \$5M capital grant from the Massachusetts Life Sciences Center (MLSC) in 2015 to expand microbiome resources in the state."

Bry encourages investigators interested to commercialization to consider the broad applications of their work, not only in Partners HealthCare, but in other settings as well.

"Commercializing a new idea requires thinking about things in ways that differ from how you would write a grant or manuscript for publication. Be open to pursuing different methods of funding an idea and working with individuals who have expertise in areas outside of basic or clinical research."

Since AI is a relatively new term in the field of biomedical research, the IDG team is anticipating receiving a lot of questions from applicants, says Lesley Watts, who manages IDG program. The good news is that the field is fairly broad.

If you're not sure if your idea falls into one of these fields—or if it is far enough along to seek grant funding—it is still a good idea to reach out, says Watts.

Watts, who is part of the Partners Innovation team, has compiled a list of contacts that members of the Partners HealthCare community can access to discuss their ideas and identify possible next steps.

“We included all the resources that investigators could turn to and say, ‘I know there is a good idea in here—I just don’t know what to do with it or how to make it into a reality.’”

The listing includes representatives from seven centers in the Partners HealthCare system with expertise in AI and machine learning as well as individual subject matter experts who can serve as a first point of contact.

“Reach out and access these resources,” Watts says. “Whether or not your idea turns into an IDG grant or a full application, it can start a conversation and point you in the right direction.”

“There are all kinds of different takes on it. We expect radiology and pathology to be well-represented among the applicants, but we have people from psychology and technicians who are planning to apply.”

Watts says the IDG Program has rated very highly with the investigators who have participated in it over the past two years. During two earlier rounds of the IDG Program, \$2M dollars was awarded to 30 promising projects. More than 550 initial proposals were submitted in prior rounds.

For more information about the IDG program and to access AI resources, please visit [innovation.partners.org/about/special-programs/partners-innovation-development-grants-program](https://innovation.partners.org/about/special-programs/partners-innovation-development-grants-program). ■



# Technological Advances Powering New Insights into the Human Microbiome

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This is the first article in a series about research related to the human microbiome at Partners' academic institutions. We talk to Lynn Bry, MD, PhD, from the Department of Pathology at Brigham and Women's Hospital.

If you think about it, the scientific quest to understand the human microbiome is not unlike trying to follow along with HBO's hit TV series "Game of Thrones."

The show features intricate plotlines and a wide and complex cast of characters who interact in a myriad of ways—sometimes working together, sometimes at odds with each other. The lines between the heroes and villains are frequently blurred, and at any moment, a sudden unexpected event can throw everything into chaos.

While it may lack the swordplay and special effects, the study of the microbiome—the interactions between humans and the trillions of microorganisms that live on and within our bodies—has revealed its own web of complex relationships and ever-shifting power balances.

In many cases, the microbiota in our bodies play a crucial role in keeping us healthy, assisting with everything from digestion to ensuring our immune system operates effectively.

In other cases, however, they can be harmful. Imbalances or disturbances in the microbiome can lead to food allergies, infections, and chronic inflammatory conditions, and when it comes to conditions such as *C. difficile*, the stakes can literally be life or death.

Researchers in the academic medical institutions of Partners HealthCare are using a variety of innovative strategies to learn more about how the microbiome works and what happens in different disease states. It's a massive undertaking with the potential to make a major impact on patient care.

## The Technological Push

Given all the attention it has received in recent years, it may seem like the microbiome is a brand-new area of scientific investigation. In fact, research into the differences between colonies of microbiota in humans dates back to the late 1600s.

Dr. Bry , Director of the Host Microbiome Center at BWH, says recent breakthroughs include the introduction of technologies such as next generation sequencing and high throughput proteomic mass spectrometry. These tools have provided researchers with unprecedented insights into the composition of microbes at the genetic level.

The technologies also make it possible for researchers to observe how an individual's microbiome changes over time and how it reacts to different perturbations.

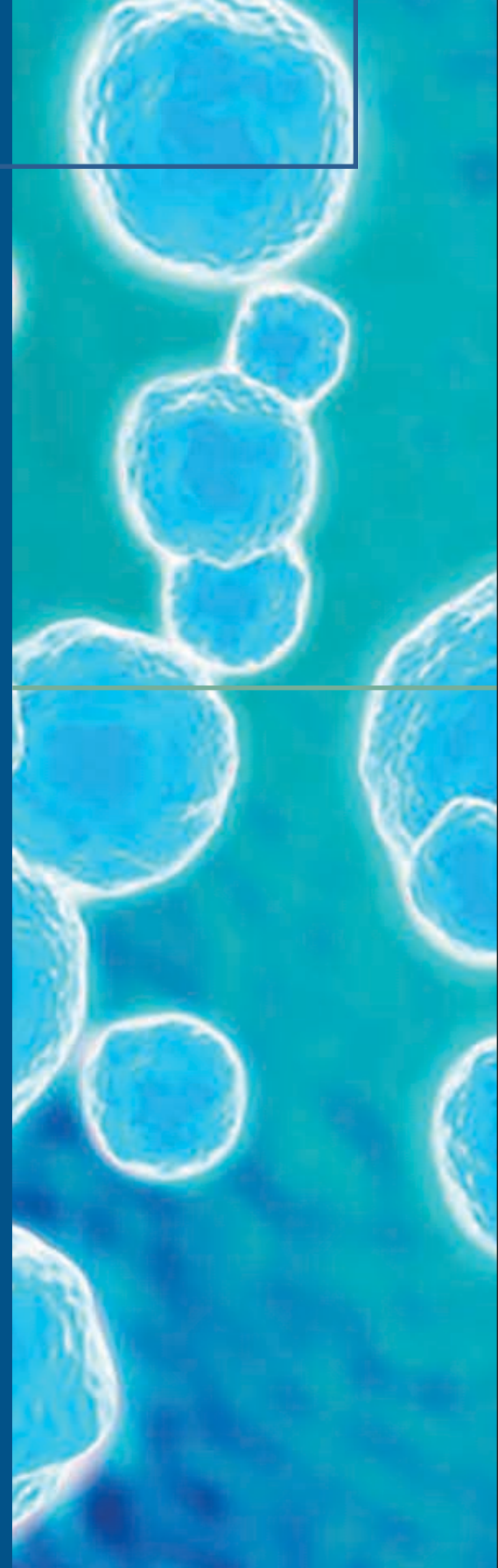
"We can now distill a complex ecosystem into a subset of component microbes we think are important," Bry says, "and then go back to experimental systems to understand the dynamic and what's truly driving what in the system."

For Bry, who has been studying interactions between microbes and the cells of the human intestine since the 1990s, these breakthroughs helped inform new approaches to identifying what goes wrong in conditions such as treatment-resistant *C. difficile*, inflammatory bowel disease, food allergies and more.

### **Seeking New Solutions for *C. Difficile***

Bry and her team are particularly interested in learning the mechanisms behind treatment-resistant *C. difficile*, a potentially life-threatening infection that's particularly harsh on patients over the age of 65, especially those in hospitals and nursing home settings. A 2015 research study estimated that the cost of treating the condition is \$6.3 billion per year.

*C. difficile* is an infection caused by the pathogenic bacteria *Clostridium difficile* that results in inflammation of the intestines and severe diarrhea. Patients taking antibiotics for other conditions are most susceptible as they can alter the balance of microorganisms in the body, which creates opportunities for *C. difficile* to attack.



According to the Centers for Disease Control and Prevention (CDC), there are 500,000 cases of *C. difficile* contracted in the United States each year, and the infection becomes recurrent in about 20 percent of those patients, which can lead to frequent and debilitating attacks.

According to the CDC, one in 11 patients aged 65+ will die within a month of receiving a *C. difficile* diagnosis, and 80 percent of all *C. difficile*-related deaths come from the patients in this age group.

At BWH, Bry is part of a precision medicine project seeking to identify biomarkers that indicate which patients are at greater risk of recurrent *C. difficile* infections and why. It's a problem that will likely take many different tools to resolve.

"It's the combination of having the experimental system with the high throughput platform, the computational algorithms, the back and forth between what you are able to learn at the bench with what you're able to learn in silico," Bry explains. "Certainly, we've had the best success when we compare [our results] to the patient population."

"We need to understand what is out of balance and then understand what we can do about it."

Bry hopes that research into *C. difficile* and other areas of the microbiome will lead to a new range of treatment options for patients. This could include changes in diet, ingestion of modified microorganisms (so-called bugs with drugs), and the development of new molecular therapeutics, among others.

Industry partnerships will play a key role in developing these therapies and bringing them to market, she adds.

"We know we are not optimally positioned to commercialize [new therapeutics], so we would certainly want to forge collaborations with industry to make use of them, get clinical trials going and see what we can use in the clinic."

And just like the many unexpected plot twists on "Game of Thrones," the more researchers learn about the microbiome, the more questions are sure to arise. ■

The breakthroughs and capabilities developed at Partners HealthCare by its 3600 Harvard Medical School Medical School appointed faculty and employees at its core academic hospitals—Brigham and Women’s Hospital, Massachusetts General Hospital, McLean Hospital, and Spaulding Hospital—are reshaping modern medicine and improving the lives of millions of patients and their families worldwide. Partners Innovation is responsible for enabling commercial application, growing Partners collaborative innovation capacity and advising international organizations seeking to improve care.



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