BRI RACES TO UNDERSTAND COVID-19

BRI scientists were sure of one thing when the coronavirus struck: They had the expertise to make swift progress toward understanding it and finding better treatments.

“Studying how the immune system responds to viruses has been part of our work for years,” says BRI president Jane Buckner, MD, “so we were ready to play a key role in fighting COVID-19.”

It normally takes years to fund and launch major research, but our team has kicked off several studies in a matter of weeks. We’re investigating some of COVID-19’s biggest questions and pursuing answers that could stop it in its tracks. These promising studies are partly funded by an amazing community of donors that stepped up with gifts to our COVID-19 Rapid Response Fund when we needed them most.

“The virus is so new that our research is like solving a jigsaw puzzle, except we don’t know where the edges are or what the picture looks like,” says BRI affiliate investigator Matt Altman, MD, MPhil. “We have to start from nothing and learn everything we can, as fast as we can.”

KEY PARTNERSHIP

It’s easy for BRI researchers to see their work’s potential impact: Our main building is across the street from Virginia Mason Medical Center, where dozens of patients have come for COVID-19 treatment. Some of these patients have mild symptoms and get better on their own, while others need critical care.

BRI and Virginia Mason quickly launched research to understand why the virus affects people so differently. This research capitalizes on our decades of experience recruiting patients and investigating immune activity. And it wouldn’t have been possible without private donors.

“We’re using blood samples from Virginia Mason COVID-19 patients to study several key questions,” says Cate Speake, PhD, “and we hope this leads to a test that could predict if a patient will have severe symptoms, so their doctors can be ready with the right treatments.”

POTENTIAL THERAPIES

When the National Institute of Allergy and Infectious Diseases (NIAID) launched a study examining how the immune system reacts to the new

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coronavirus, they wanted Dr. Altman and Scott Presnell, PhD, on their team. The scientists had developed a way to collect samples and analyze millions of data points from respiratory samples in asthma patients — and their method could shed light on COVID-19.

Dr. Altman and Dr. Presnell received a $2.6 million grant as part of a larger study where BRI is among 10 institutions analyzing about 2000 samples. Approximately 6,000 samples will be analyzed at BRI. That’s no small task: Each sample holds as much information as a lengthy novel.

“We sometimes make the analogy that it’s like reading ‘War and Peace’ thousands of times and looking for typos,” Dr. Altman says.

That’s where Dr. Presnell comes in: He uses bioinformatics to quickly sift through that information and pinpoint which genes are turned on and off in the body’s airway during COVID-19.

“This should illuminate which genes are responding to COVID-19 and it could lead to therapies that affect those genes so more people can overcome the virus,” Dr. Presnell says.

HOW DOES COVID-19 AFFECT LUNGS?

Steven Ziegler, PhD, is also investigating how the body fights off COVID-19. He studies epithelial cells in the lungs, which form the barrier between us and the outside world. These are the cells that respond to invaders like viruses, but they can mistakenly overreact to things like pollen.

“We’re studying how your body decides what to fight and why it can go wrong,” Dr. Ziegler says.

Dr. Ziegler’s team recently earned a grant to add COVID-19 to their research on asthma. Using a model that he likens to “a lung in a dish,” his team will examine how immune cells respond to the virus.

“This will help us understand what a healthy response looks like and how we might help people who don’t have a healthy response,” he says.

WHEN DO VENTILATORS HELP?

Long before the pandemic, Carmen Mikacenic, MD, had to tell many patients and families that going on a ventilator was their only hope — and there was no way to predict if it would work. Many patients with severe COVID-19 are hearing the same thing, and Dr. Mikacenic wants to give them better answers.

Dr. Mikacenic, BRI’s newest principal investigator, is a pulmonologist and critical care doctor. She treats patients with lung problems like acute respiratory distress syndrome (ARDS). This condition occurs when fluid collects in the lungs, making it hard or impossible to breathe. It’s also a common COVID-19 complication.

“We put patients on ventilators to support them while their body fights off the disease, but we don’t...
We'd like to extend a special thanks to community members who have made financial gifts to BRI’s COVID-19 Rapid Response Fund.

We have raised more than $350,000 and counting.

Your generous support makes this research possible!

have therapies to fix the underlying condition,” Dr. Mikacenic says.

That’s why she’s on a quest to investigate ARDS and find new treatment options. She’ll be receiving a grant to learn more about how ARDS affects patients, including those with COVID-19.

“When someone develops ARDS, I want to be able to tell their family if a ventilator will help and, eventually, that we have a treatment to address what’s causing their lung problem,” Dr. Mikacenic says.

BRI AS PART OF THE SOLUTION

Not only have BRI scientists launched these studies rapidly — they’ve done this by working seven days a week, often from home. While COVID-19 still holds many mysteries, our team is agile and knows how to lean into a scientific challenge.

“Every day, we chip away at scientific mysteries and for diseases like multiple sclerosis and diabetes — and we believe we can achieve cures,” Dr. Speake says. “That’s why I know we can help with COVID. Our team and the scientific community at-large have come together, and we’re giving everything we have to fight it.”

CARMEN MIKACENIC, MD

Dr. Mikacenic joins us from UW Medicine to continue her research on acute respiratory distress syndrome (ARDS). This serious lung illness affects 150,000 people in the U.S. each year — including many people with the worst cases of COVID-19. She also studies interstitial lung disease, a complication of multiple autoimmune diseases where patients develop inflammation and scarring in their lungs.

“I’m excited to work with BRI’s team of world-class immunologists to pursue desperately-needed new treatments for these conditions,” she says.

HAMID BOLOURI, PHD

Dr. Bolouri joins BRI’s Center for Systems Immunology Division from the Allen Institute for Immunology. He is assisting with multiple research projects across BRI and pursuing questions of his own. For Dr. Bolouri, one of the most intriguing questions is whether we can create complete data profiles of people with healthy immune systems and people with autoimmune diseases.

“Documenting the immune system in this way — similar to documenting the human genome — would open up so many pathways for treating and curing autoimmune diseases,” he says.
Peter Linsley, PhD, hit a crossroads in 2012: After years in the private sector, he wanted to get back to moving medicine forward.

“I called BRI because I saw an opportunity to study autoimmunity in a whole new way,” he says.

BRI’s then-president, Jerry Nepom, MD, PhD, knew Dr. Linsley was pioneering a “systems” approach that examines how myriad factors conspire to cause disease. Dr. Nepom also knew that Dr. Linsley’s research helped spawn breakthrough cancer treatments.

Dr. Nepom wanted similar progress against autoimmune disease, and he was intrigued by making BRI one of the first to embrace the systems approach. So he offered Dr. Linsley a job.

Eight years later, BRI is home to a Center for Systems Immunology that is helping us investigate the immune system’s deepest mysteries and the riddles of COVID-19.

“Our systems immunology team has become indispensable to understanding complicated diseases and pursuing better treatments,” says BRI’s current president, Jane Buckner, MD.

A BROADER PERSPECTIVE

Immunology researchers traditionally focus on something narrow — such as a type of cell or a pathway within that cell — and learn everything possible about it. The systems immunology team examines how those elements interact with dozens of other factors, including things like age and gender.

“The traditional approach is like looking for keys under a streetlamp,” Dr. Linsley explains. “Systems immunology takes you out wider to see what’s in the shadows.”

Combining these approaches has led to key insights. For example, Dr. Linsley and his colleagues collaborated with Alice Long, PhD, to identify potential new approaches to treating type 1 diabetes (TID).

“There are many factors that contribute to TID,” Dr. Long says. “The systems immunology team helps identify which ones are important.”

BIG DATA AND THE BIG PICTURE

The systems immunology team of bioinformaticians and data specialists uses the latest cloud computing tools to organize, analyze and visualize the vast amounts of data in blood and tissue samples.

“Finding patterns across millions of data points is tremendously complicated, but that’s kind of our superpower,” says Charlie Quinn, who is director of the research information systems team.

Having the team in-house means it can join forces with people like Dr. Long early in the research process, to be sure everyone knows which patterns to look for. This helps researchers understand autoimmune responses and investigate how to correct them.

INVESTIGATING COVID-19

Dr. Linsley and his colleagues — including Hamid Bolouri, PhD, Scott Presnell, PhD, and Matt Dufort, PhD, are using systems immunology tools to study multiple COVID-19 questions.

One goal is to find markers that identify why some people with the virus don’t have symptoms while others get fatally ill.

“That is precisely why systems immunology is necessary — we can find meaningful patterns in a sea of noise,” Dr. Bolouri says. “Once we know what the markers are, we can look at the different ways the virus affects people, identify what goes wrong in their immune processes, and tailor treatments to individual patients.”

BRI’s ability to comprehensively study COVID-19 achieves the vision that Dr. Nepom and Dr. Linsley hatched back in 2012.

“We have the pieces in place to jump into action and make discoveries that can help,” Dr. Linsley says. “That’s exactly what you hope for as a scientist.”
10-YEAR-OLD CELEBRATES RESEARCH

It might seem strange for a kid to be sad they can’t get poked with needles. But for Zoe Brooke, age 10, having her visits to BRI’s Diabetes Clinical Research Program canceled has been one of the most frustrating parts of the pandemic — right up there with having to change her birthday party. Zoe lives with type 1 diabetes (T1D) and has participated in BRI research for nearly half her life.

“Anna asks if I have questions about Zoe’s blood sugar or if I need support,” says Kari, Zoe’s mom. “As a parent, that’s an incredible resource.”

Zoe’s passion for research is clear: She has stuffed animals named after BRI’s team and loves doing pretend blood draws on her mom.

“Anna teaches me stuff and lets me help take my temperature,” Zoe says. “They gave me a badge that says ‘Zoe Brooke, Junior Nurse.’ I want to be a real research nurse when I grow up.”

BUILT-IN RESILIENCE

Anna also manages her own T1D and, during the pandemic, she’s been one of a handful of BRI nurses spending extra hours helping Virginia Mason field calls from people with COVID-19 symptoms.

“Diabetes teaches you to live with the unexpected — we’re used to constant change,” Anna says. “People with chronic illness have this built-in resilience, and we can really tap into that in moments like this.”

Zoe is living proof. She has some advice for people to get through difficult times, whether or not they have T1D.

“I feel happy because I know I can have a challenge in my life and get through it, even if it’s hard, or scary, or other people thought I couldn’t,” she says. “When the world tries to push you down, keep your head up and keep moving forward.”

10-YEAR-OLD CELEBRATES RESEARCH

Anna Barash and Zoe Brooke after Zoe became the first participant to enroll in the PROTECT study.

“I want to help researchers get closer to a cure, so people won’t have to be scared if they get diagnosed,” she says.

For Zoe and other research participants, BRI’s studies are a concrete way to fight their disease — and they take pride in knowing their participation can help so many others. Zoe participates in the PROTECT study, which examines whether an immunotherapy drug called teplizumab can slow T1D in recently diagnosed patients. However, this trial and several others have been postponed until trials can safely reopen due to COVID-19.

Still, Zoe is doing everything she can, and BRI’s clinical research team is supporting her and other participants from far away.

“We get so close with these families and we’ve found ways to continue that support from a distance,” says BRI Clinical Research Nurse Anna Barash, RN, DCE.

SUPPORT FROM A DISTANCE

For instance, Anna’s team monitors participants’ blood sugar remotely and keeps in touch over the phone.

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Status of Clinical Trials

To mitigate the spread of COVID-19 we put in-person research participation and some clinical trials on hold during Phase 1 of the governor’s Stay Home Stay Healthy orders. As we moved into Phase 2, we have followed Virginia Mason’s lead and have begun seeing research subjects again using increased precautions.

We are recruiting participants for the Sound Life Project and patients who have recovered from COVID-19. Patients visiting Virginia Mason clinics can participate in some projects, for example joining a biorepository. Some clinical trials are underway while others remain on hold. If you are a research participant and have questions, contact your study doctor or research coordinator, or email CRP@benaroyaresearch.org.
Inside BRI’s Race to Understand COVID-19
It normally takes years to launch major research, but BRI kicked off COVID-19 studies within weeks.

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A 10-Year-Old Is Committed to Research, No Matter What
Zoe Brooke has persevered through COVID-19 and found ways to stay involved in our research.