A Letter From Our President: Latest Advances at BRI

We’ve been living in a world of COVID-19 for over a year. In the face of a pandemic, BRI’s vision — a healthy immune system for everyone — has become more important than ever. We’re so thankful for the incredible support from you, our community. And I’m excited to update you on our work and introduce our new brand.

Over the past year, BRI’s team, including three new principal investigators, have used our tools and expertise to unlock some of the mysteries of COVID-19. From home offices and socially distanced labs, we’ve continued studies that shed light on everything from Crohn’s disease to cancer. We’ve helped test a breakthrough vaccine. And we’ve pushed forward with the Sound Life Project, helping us better understand what constitutes a healthy immune system, how or why imbalances happen and, perhaps most importantly, how we can reset it back to health.

No matter how long it takes to get back to normal, BRI will continue our quest to predict, prevent, reverse and cure immune system diseases. This commitment is reflected in our new brand: Powering Possibility.

Powering Possibility encompasses BRI’s commitment to creating a world without immune-related diseases.

This means a world where no one has to plan their lives around insulin injections or scrutinize every meal for allergens. It means a world free from the pain, limitations and social stigma associated with immune diseases, from rheumatoid arthritis to multiple sclerosis.

Every BRI study, discovery and innovation powers possibility by moving us toward this world. Each study may not result in a life-changing discovery. But all studies fuel progress that ultimately informs the quest for prevention and cures by opening the door to new questions and new advances.

COVID-19 has brought the global research community together, focusing on the immune system and working quickly and collaboratively. If we can continue at this rate with a sustained focus on immunology, we will be closer to finding ways to rebalance the immune system back to health — or better yet, a world where healthy immune systems stop disease before it starts.

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Testing a Vaccine That’s Changing the World

In August 2020, BRI Research Nurse Anna Barash, RN, gave some of the earliest doses of Pfizer’s COVID-19 vaccine to people in Washington. That day, she was laser-focused on following every step of a detailed protocol. The impact of her work didn’t sink in until later.

“I remember getting home that night and thinking ‘this is monumental,’” she says.

Anna is part of a BRI clinical research team. For decades, this team has run trials typically focused on type 1 diabetes. But COVID-19 forced the suspension of many of those studies – leaving BRI with an expert team and fewer trials to run. Around that time, Pfizer was preparing to test a potentially groundbreaking vaccine. So Carla Greenbaum, MD, director of the Center for Interventional Immunology and the Diabetes Research Program, reached out.

“The whole world was reeling from the pandemic,” Dr. Greenbaum says. “Our team had the availability and the skill set; we know how to run trials and we run them very well. So, I emailed a contact at Pfizer who connected me to someone else – and BRI became their only vaccine testing site in Western Washington.”

“When I got the vaccine, I had this intense feeling of pride. This work is saving people’s lives. And to receive the product that we worked so hard on, that’s a once-in-a-lifetime opportunity.”

—Kim Varner, Manager, Center for Interventional Immunology

Special thanks to the BRI team members who made this study possible:

Our clinical research team, led by Sandra Lord, MD, and including research nurses Barbara Booth, RN; Anna Barash, RN; Kristal Liu, RN; and MacKenzie Robinson, RN

Our clinical coordinators and research assistants: Corinna Tordillos, Kim Varner, David Kook, Rishab Kotak and Rachel Hartley
TESTING A VACCINE

THREE WEEKS, 160+ DOSES, 6 FEET APART

Dana VanBuecken, ARNP, a sub-investigator on the Pfizer study, remembers the exact moment she learned BRI would be a testing site.

“I had this immense feeling of excitement and gratitude to play just a small part in the solution to the pandemic,” she says. “This year has been hard for everyone, but contributing to this trial gave me a tremendous sense of hope. I had so much faith in our team.”

BRI was one of about 150 Pfizer testing sites across six countries and 39 states. First, researchers opened enrollment for the trial and spread the word that they were looking for volunteers to participate in the study. Some participants would receive the vaccine, others would receive the placebo.

“Everybody wanted to participate — we could have enrolled ten times as many people,” says Dr. Greenbaum, who led BRI’s arm of the study. “We needed frontline workers to enroll, and several Virginia Mason ER doctors and those from other local hospitals were excited to get involved.”

Then came the jigsaw puzzle of logistics: They had only three weeks to give the first vaccine dose to over 80 participants — and maintaining social distancing meant they could have only a handful of people in BRI’s Clinical Research Center at a time. The research team mapped out detailed plans and schedules and worked nights and weekends to make this happen.
“This experience taught me that if something looks impossible, it’s probably not with this team,” says Research Technician Rachel Hartley.

At the end of each day, they followed another detailed protocol: They entered data about potential COVID-19 illnesses and vaccine side effects, being monitored closely by Pfizer.

“I entered the data every single day,” Rachel says. “I saw the safety measures in place and know that every box was checked, and every precaution was taken. That’s made me really confident in telling family and friends that this vaccine is a good thing and we’re really proud to be part of this work.”

MAKING A DIFFERENCE

After weeks of long hours, the team had given two doses of the vaccine or a placebo to 82 participants. Next, they waited: for enough data to be collected worldwide, for Pfizer to announce whether its safety and efficacy endpoints had been met, and for the FDA to independently review the data and decide whether to authorize the vaccine for emergency use.

“During that time, I kept thinking of this Thomas Edison quote that’s something like ‘I never once failed at making a lightbulb. I just found out 99 ways not to make one,’” Dana says. “That’s often how research works — and each attempt is important — but of course we really wanted this to work.”

In late 2020, the research team finally got an email from Pfizer: The FDA approved the vaccine for use during the pandemic emergency. In that moment, all of the long hours were worth it. Shortly after, Dana got a text from her sister, an ICU nurse in California.

“She sent me a picture of herself getting the Pfizer vaccine and I broke down and cried,” Dana says. “I’ve been so worried about her and others in similar roles, putting their health on the line to care for others. It’s been so gratifying to help take this vaccine from an idea to something that’s truly making a difference. It’s incredible that BRI has played a role in that.”
Understanding What Causes IBD

James Lord, MD, PhD, has a simple way of explaining the immune system.

“It’s not a homogenous pot of stew,” he says. “It’s a carefully orchestrated dance, and doing the right thing at the right time is critical. But it’s very hard to predict the choreography.”

Dr. Lord — with Amiko Uchida, MD; Elisa Boden, MD; Eddie James, PhD; Donna Shows; and Andrew Konecny — recently published a study that revealed a small but vital piece of this immune system dance. Their findings concern a protein called interleukin 10 (IL-10), which plays a key role in preventing gut inflammation. Scientists have tried using it to stop the inflammation that causes inflammatory bowel disease (IBD) — and it’s never worked.

“Scientists tried injecting patients with IL-10 and it didn’t do anything,” Dr. Lord says. “They tried using bacteria that make IL-10, but that didn’t do anything either.”

Years after these attempts from other scientists, Dr. Lord and his team stumbled upon this protein again when studying an unusual immune response in some people with Crohn’s disease. Their findings could shed light on how IBD happens and when IL-10 needs to present to prevent the inflammation of Crohn’s disease.

“You can’t use IL-10 as a crude sledgehammer to knock down the immune system,” Dr. Lord says. “But if it’s given at exactly the right time, by exactly the right cell, responding to exactly the right antigen, it can prevent gut inflammation that contributes to IBD.”

**FINDING THE PERFECT CONTEXT**

The investigation started when researchers ran into a mystery: In some people with Crohn’s disease, the immune system reacts to E. coli, a common gut bacteria, by making antibodies to one of its proteins called OmpC.

“Everybody’s colon is full of E. coli,” Dr. Lord says. “So, you shouldn’t have a colon immune response to OmpC, but at least half of people with Crohn’s disease do.”

To find out why, researchers compared blood cells from people with Crohn’s disease to blood cells from people who were genetically similar but didn’t have Crohn’s disease.

They found that people without Crohn’s disease had T-cells that could recognize OmpC as foreign but these people didn’t make antibodies to the protein. Instead, their T-cells made a lot of IL-10, a protein known to decrease immune reactions.

Meanwhile, T-cells from people with Crohn’s disease made little to no IL-10. They also had antibodies to OmpC — a telltale sign that the immune system had attacked.

This led the research team to suspect that IL-10 needs to be made by the right immune cells at the right time and place to successfully prevent inappropriate gut inflammation.
“Determining why these immune cells don’t make IL-10 when they encounter normal gut bacteria, like E. coli, could explain how IBD happens and inform how and when IL-10 needs to be present to prevent the inflammation of Crohn’s disease,” Dr. Lord says.

**CHAIN REACTION CAUSES DISEASE**

Next, the research team plans to study the gene that makes IL-10 in extreme detail, to learn why it doesn’t work properly in some people with Crohn’s disease. They’ll look for differences in tiny molecules, which could provide insight into the chain reaction that causes the disease. If they can understand how that reaction starts, they may be able to stop it — and prevent the disease.

This approach is called a reductionist model, which means looking at the smallest parts of something to understand the whole.

“We’re looking at one peptide from one protein from one class of bacteria in one fairly common but still genetically distinct subset of Crohn’s patients,” Dr. Lord says. “It’s extremely reductionist, but that’s how science happens. If we find differences in these very specific cells, that may be true for all cells in Crohn’s. We’re trying to leapfrog from a reductionist model back to something broadly generalizable.”

These findings could go beyond Crohn’s disease and launch more questions: Does this chain reaction also keep IL-10 from stopping inflammation in ulcerative colitis and celiac disease? Is it part of the mechanism behind all autoimmune diseases?

“One of BRI’s mottos is that a breakthrough in one autoimmune disease can lead to a breakthrough in them all,” Dr. Lord says. “We typically find the same mechanisms work across the body, regardless of organ system. And I think we’re one of the only institutions on Earth that is so equipped to study multiple autoimmune diseases in parallel at such depth.”

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**Support IBD Research By Joining Our Biorepository!**

BRI supporters who live in and around Seattle can fuel our research by donating blood and biologic samples to our biorepositories. Scientists study these samples to learn more about immune-related diseases like IBD. All information gathered is confidential. Our IBD biorepository is open to people 16 and older, including:

- People who live with Crohn’s disease, ulcerative colitis and indeterminate colitis
- First degree relatives of participants with disease
- Individuals with non-IBD causes of GI inflammation, such as celiac sprue, eosinophilic esophagitis, infectious gastroenteritis or colitis

BRI has biorepositories for many other conditions, including asthma, multiple sclerosis and type 1 diabetes. People who don’t have an immune-related disease can donate to our healthy control registry. Learn more at Benaroyaresearch.org/JoinResearch.
Join Us for Science Fridays!
Everyone is invited to attend BRI’s virtual Science Fridays. These quarterly events, led by researchers and focused on the immune system, provide a firsthand look at BRI’s leading immunology research. Join us to learn and get your questions answered.

Save the 2021 dates:
May 21 | July 30 | Oct 8
12 to 1 pm PST

Attendance is free but registration is required. To learn more about Science Fridays, visit BenaroyaResearch.org/ScienceFriday. We hope to see you there!

Latest Advances at BRI
CONTINUED FROM FRONT PAGE

Many members of BRI’s community are wondering how the recent Virginia Mason – CHI Franciscan merger forming Virginia Mason Franciscan Health affects our work. The answer: BRI will keep doing research as usual. We’ll continue to work with clinicians and patients at Virginia Mason Franciscan Health as well as experts nationally and worldwide.

Our community plays a key role in this work and we couldn’t do it without you. Thank you for your steadfast support during a year like no other. Through volunteering, participating in research and making financial donations, you help us power possibilities every day.

—Jane Buckner, MD
BRI President

BRI President Jane Buckner, MD
What’s Inside

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Understanding What Causes IBD
Learn about a link between gut bacteria and the immune system that could explain how IBD starts.