Benaroya Research Institute at Virginia Mason (BRI) has made game-changing discoveries and significantly expanded our research and funding in recent years. This progress – combined with welcoming Jane Buckner, MD, as president – inspired us to update our strategic plan and embrace a broader vision: Create a healthy immune system for every individual by pursuing better ways to predict, prevent, reverse and cure immune disorders.

This vision extends far beyond autoimmune disease and is the next step in an evolution that started more than 30 years ago. BRI initially focused on type 1 diabetes (T1D) and gradually expanded to study other diseases. This led to a key insight: A wide variety of disorders are triggered when the immune system falls out of balance.

“A balanced immune system knows when and how to attack bacteria and other threats,” Dr. Buckner says. “When the immune system becomes imbalanced, it might overreact to harmless substances and cause allergies, mistakenly attack healthy cells to cause autoimmune disease, or fail to hunt down cancer cells.”

Our new plan positions us to pinpoint why immune imbalances occur, and to pursue treatments that return the immune system to a healthy state.

“BRI is home to world-renowned experts of the immune system, and our updated strategy helps us apply that expertise in new directions,” Dr. Buckner says. “This will accelerate progress toward breakthrough diagnostic tests, prevention strategies and therapies that help many more people live longer, healthier lives.”

NEW PARTNERSHIP

One key strategic goal is to create a detailed portrait of what healthy immune systems look like, so we can understand how they fall out of balance.

To do this, we’re expanding our push to recruit healthy people to donate blood to our biorepositories. Our investigators study these samples to identify a wide range of healthy immune systems.

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We also recently announced a potentially game-changing partnership with the new Allen Institute for Immunology. Fueled by a $125 million gift from the late Paul Allen, this partnership unites five top research organizations around the goal of understanding how the immune system functions. The partners include BRI; Fred Hutchinson Cancer Research Center; the University of California San Diego; the University of Colorado Anschutz Medical Campus; and the University of Pennsylvania.

BRI’s role includes creating the most detailed portrait yet of the immune system in healthy people. We’ll also study samples from individuals aged 25 to 35 and 55 to 65, analyzing changes over time.

“We’ll be able to see how healthy immune systems change as people age, and how lifestyle and environmental factors alter immune systems,” Dr. Buckner says. “This will help us understand which changes are normal and which ones contribute to disease.”

**INNOVATIVE THERAPIES**

This will set the stage for understanding how and why immune systems fall out of balance and move us closer to another strategic goal: Find ways to restore balance and stop immune-related diseases at the source.

Complex problems often require collaborations to solve them, and BRI is already partnering with pharmaceutical companies to investigate and test a new wave of immune therapies. This helps ensure these therapies are safe and effective. It also gives our researchers insights that help them pursue better ways to stop disease.

“We’re moving closer to therapies that restore balance by helping the immune system calm down and stop autoimmune diseases and allergies, or helping it ramp up and attack cancer,” Dr. Buckner says.

**GOOD TO GREAT**

Our strategic plan also includes other important elements, such as creating four new “centers of excellence that make it easier for researchers in different areas to work together. This shortens the path to discovery by helping us investigate scientific questions from every angle. It also enhances the collaborative culture that has helped BRI come so far so fast.

“BRI has played an outsize role in improving prevention and treatment of diseases like T1D and food allergies,” Dr. Buckner says. “We’re excited to make similar advances for many more diseases and to continue becoming one of the world’s great research institutes.”

*Related Article: See how Bernard Khor, MD, PhD, is pursuing ways to disarm genes that cause autoimmune diseases on page 3.*
When her son was born with Down syndrome (DS) in 2002, Rebecca Partridge, MD, couldn’t find a pediatrician to provide specialized care. So she did what any pediatrician mother would do: She started the Seattle area’s first DS clinic.

About 400,000 Americans have DS, a genetic disorder that occurs when people have an extra copy of the 21st chromosome. It leads to developmental challenges and other health issues, and almost half of DS patients have autoimmune diseases – but no one knows why. And considering the increased lifespan of people with DS, autoimmune disease is becoming an even bigger factor to contend with.

That’s why Dr. Partridge, who directs Virginia Mason’s DS program, and BRI’s Bernard Khor, MD, PhD, are leading one of the first studies that investigates autoimmunity in people with DS.

“If we can figure out when and why people with DS get autoimmune diseases, we’ll be able to treat those conditions better and maybe even prevent them – in people with DS and potentially in everyone,” Dr. Khor says.

“People with DS have extra copies of DYRK1A, and Drs. Khor and Partridge are using the biorepository to learn more about it. "If we can help people with DS balance their immune systems by blocking this gene, the same approach might work for other people too," Dr. Partridge says."

Dr. Partridge isn’t only a co-investigator for the study – she and her son are participating in it by donating samples to the biorepository.

“BRI has done a great job of making sure this study is done appropriately and for the right reasons;” she says. “We want to help people with DS live happy and healthy lives. And if we can help everyone else with an autoimmune disease, that would be even better.”

"This helps us understand what healthy immune systems look like and identify what’s different in patients with DS," Dr. Khor says. “It also gives us clues about what makes people with DS more susceptible to autoimmune disease.”

**PURSuing TREATMENTS**

Dr. Khor hopes this research leads to better therapies for autoimmune diseases or even ways to prevent them. He already has an idea for how to do this.

In a previous study, Dr. Khor found that blocking a gene called DYRK1A significantly reduces the activity of white blood cells. This led him to believe the gene might contribute to autoimmune disease, which is triggered when certain immune cells are overactive.

"By studying the immune systems of people with Down syndrome, Bernard Khor, PhD, is working to solve some of the biggest mysteries about autoimmune diseases."

**UNIQUE BIOREPOSITORY**

Last year, Dr. Khor received a National Institutes of Health grant for this study. The grant helped him start building one of the nation’s first biorepositories of blood samples from people with DS.

Dr. Khor’s team will use these samples to analyze immune cells from patients with DS and patients with both DS and autoimmune disease. The researchers will compare their findings to samples from the patients’ healthy family members.

"To learn more about the Down Syndrome Biorepository and to enroll in studies, visit www.benaroyaresearch.org/down-syndrome"
Silas Palmisano was born with Down syndrome – and diagnosed with Crohn’s disease more than a decade later. “He was so sick he missed a month of school,” says Lynne Palmisano, Silas’s mom. “He’s been on three different medications, but he’s getting worse not better.”

Dr. Partridge invited Lynne and Silas to participate in BRI’s new autoimmunity study, which aims to help improve treatment for patients like him – and potentially for everyone with autoimmune disease. “Silas never complains, but I know he’s in pain,” Lynne says. “We’re excited about helping doctors find better treatments.”

When Ryan Sinit was 8 years old, he and his family went to Thailand to visit relatives. During their trip, Ryan helped his mother crush peanuts as they prepared a meal – and quickly felt his throat swell until it was hard to breathe. Fortunately, Ryan’s mother had easy access to an EpiPen and delivered a quick injection. But Ryan, who also has exercise-induced asthma, still has to be on guard for peanuts. That’s why he joined a BRI study that investigated whether gradual exposure to peanut protein could make patients more tolerant and make reactions less severe.

“The selling point was my love for travel and concern about food safety when eating out,” Ryan says. As Ryan participated in the study, he took a job as a coordinator in Virginia Mason’s cancer clinical research program, which is overseen by BRI.

Today, Ryan coordinates several cancer studies that investigate how patients tolerate new medications. He’s also applying to medical school, and his experience with clinical research will broaden the perspective he brings to patients. “You hear about incredible breakthroughs in science and medicine, but they’re only one of many steps,” he says. “Clinical research is critically important to help us assess options and improve how things are done.”
In 2017, Eric Wambre, PhD, announced he and his team had identified a cell, called TH2A, that appears to cause all allergies – and dozens of media outlets hailed the discovery’s potential to transform diagnosis and treatment.

“Allergies happen when the body overreacts to a substance like pollen or peanuts,” Dr. Wambre says. “We found that TH2A cells help cause this overreaction.”

This opened the door to developing a test that could detect TH2A cells and identify when patients have allergies. Even better, researchers could pursue therapies that target TH2A cells and stop allergies.

It was the sort of breakthrough that scientists like Dr. Wambre dream of, but he knew it would take years to translate it into real-world progress for patients. Fortunately, he and his team are moving fast.

“We’re partnering with pharmaceutical companies to evaluate exciting new allergy therapies,” Dr. Wambre says, “and we’re exploring how drugs can block TH2A cells and maybe stop allergies altogether.”

REPLACING THE CHALLENGE TEST

Much of Dr. Wambre’s current work focuses on peanut allergies. These allergies have grown far more common in recent years, and they’re feared because they can cause life-threatening reactions. But there are no good tests or FDA-approved treatments.

“The only reliable way to know if a patient has a peanut allergy, or if their allergy is getting better, is to do a challenge test that exposes them to the allergen to see how they respond,” Dr. Wambre says.

Dr. Wambre’s lab is involved in clinical trials that suggest a TH2A-based test could be an alternative. The trials investigate therapies meant to desensitize people to the peanut allergen. His team has found that the number of TH2A cells falls in patients who respond to the therapies.

Dr. Wambre envisions a day when certain patients won’t need challenge tests – they’ll have their TH2A levels monitored instead. This could tell patients if they truly have an allergy, and if it has subsided enough for them to worry less about peanut exposure.

TH2A could also be used as a biomarker that helps match patients with therapies that are right for them.

“It could enable physicians to be much more precise about which drugs they give to patients, to make sure they get the right therapy from the start,” Dr. Wambre says.

DEVELOPING TREATMENTS

Another arm of Dr. Wambre’s research is aimed at finding treatments that disarm TH2A cells.

His team is using lab tests to investigate how existing drugs affect these cells. This will help the researchers understand how the cells work and how to use drugs to block them.

“It will probably be 10 to 12 years before there’s a therapy we can try in people,” Dr. Wambre says. “But we’re learning fast and we’re going to keep investigating until we find something that, hopefully, can help many more people overcome allergies.”

TH2A cells are home to several receptors that could be targeted by therapies.
an excerpt from the poem, *the Body Lives Its Undoing*

...I am a heaving glacier clattering tending to cacophony.
I am the kinglet droves giving way to a swelter of crows cawing.
I could be the roughened music of cells awry one gene or more
a minor-major scale a mix-tape of chaos.

Because the mayor of my body handed over
the keys to invaders I am cascading through flames
joints and muscles dragging like a loose muffler on asphalt
fighting off one illness then another ...


Join Us for Poetry Readings and Discussion Events

March 7, 7 to 8:30pm - Pacific Science Center, Seattle
Sept. 18, 7 to 8:30pm - Town Hall Seattle

Contact Christi Nichols at cnichols@benaroyaresearch.org for further information.