HOW BRI IS FIGHTING TYPE 1 DIABETES

When Merry Malnar was 11 years old, her mom took her in for a routine physical and asked the doctor to test for type 1 diabetes (T1D). Merry seemed perfectly healthy, but T1D ran in the family and her mom feared Merry would inherit it.

“That night, they called and said I had type 1 and that I needed to check into the hospital the next morning,” Merry says. “I remember the exact date — July 24, 1986 — because my life hasn’t been the same since.”

Merry spent a week in the hospital, getting a crash course in controlling her blood sugar. Now she’s guiding her 15-year-old daughter, Kayleigh, through many of the same lessons. Kayleigh has early-stage T1D and, while T1D treatment has improved dramatically in the past 30 years, the disease still comes with a litany of potential consequences, including heart disease and stroke.

That’s why Merry and Kayleigh participate in research at Benaroya Research Institute at Virginia Mason (BRI), where researchers are revolutionizing our understanding of T1D and setting the stage for game-changing treatments.

BRI President Jane Buckner, MD, “and we’re working to transform care for millions of people by pursuing everything from therapies that prevent the disease to treatments for people who’ve had it for decades.”

A HOLY GRAIL

In T1D, immune cells attack the pancreas until they destroy its ability to produce insulin — a key hormone that regulates blood sugar. As a result, people with T1D require insulin injections. BRI researchers have spent more than two decades pursuing one of T1D research’s holy grails: a way to halt the disease before insulin production stops.

Knowing that T1D runs in families, investigators from Type 1 Diabetes TrialNet — a worldwide network of researchers including many based at BRI —
took a critical first step. They conducted a study that screened more than 200,000 people with a family history of the disease. The researchers kept track of which patients developed T1D and painstakingly analyzed blood samples from each person, looking for markers that could help predict who gets the disease.

Together with results from other studies, this led to a groundbreaking discovery: The vast majority of patients who have two or more key autoantibodies (markers in the blood that signal the body is attacking insulin-producing cells) will go on to be diagnosed with the disease. This is a key insight because, for most people, T1D seems to occur suddenly, with life-threatening complications that result in a trip to the emergency room. TrialNet developed a staging classification system that can help prevent this.

Now anyone who tests positive for two or more autoantibodies can be classified as having stage one T1D. This helps doctors know when patients are in the disease’s pre-symptom stages, so they can plan treatment.

“It’s akin to how high blood pressure can predict heart attack and stroke,” says Carla Greenbaum, MD, who heads BRI’s Diabetes Clinical Research Program and leads thousands of international researchers as TrialNet’s chair.

Today, we can treat high blood pressure long before someone experiences heart symptoms or complications. The same is becoming true for T1D.

“We can match people in stage one with clinical trials of therapies that try to prevent the disease or slow it down,” Dr. Greenbaum says.

### SLOWING IMMUNE ATTACKS

The Diabetes Clinical Research Program is the overarching umbrella of BRI’s T1D research. It encompasses many BRI researchers and staff members, and is integrally connected with TrialNet and other key research initiatives.

Under Dr. Greenbaum’s direction, BRI and TrialNet are leading clinical trials that explore ways to stop T1D. The TrialNet trials take place worldwide and are supported by the TrialNet Clinical Network Hub, which is housed at BRI. We are also one of 24 TrialNet sites that offer clinical trials to patients and collect data.

These trials have the potential to transform the lives of people like Kayleigh, who tested positive for multiple T1D autoantibodies. She’s participating in blocking TSLP could potentially contain not just breast cancer, but many other tumors that have elevated TSLP — including pancreatic cancer, cervical cancer and multiple myeloma.

— Emma Kuan, PhD

BRI is moving closer to a day when we can slow down type 1 diabetes, or prevent it altogether.

— Carla Greenbaum, MD

### CLOSER TO PREVENTION

BRI’s Diabetes Clinical Research Program is involved in major research initiatives to predict, prevent, treat, halt and ultimately cure T1D. We play a key role in TrialNet, a worldwide collaboration that’s making progress toward prevention. Thanks to TrialNet’s discoveries, we can use blood tests to pinpoint who is most likely to develop T1D. This enables treatment at the disease’s earliest stage, and lets patients enroll in clinical trials of drugs that aim to stop T1D.
a TrialNet study to see if an innovative drug called abatacept can slow immune attacks and extend T1D patients’ ability to produce insulin.

“We know that producing even a little insulin can dampen T1D’s effects and help people stay healthier,” Dr. Greenbaum says, “so the longer a patient can do that, the better.”

When Kayleigh joined the study in 2017, she and Merry had to make regular 90-minute treks from their home in Port Orchard to BRI’s Clinical Research Center. Each time, Kayleigh spent two hours in a hospital bed while the drug or a placebo — she won’t know which until the study’s over — was infused into her blood. Then she and her mom enjoyed exploring Seattle before taking the ferry home.

“I’d love it if we find out I’ve been taking the drug and that it will help me stay healthier,” Kayleigh says. “But even if the study doesn’t help me, I like knowing that it gives researchers information that could eventually help other people.”

KICKSTARTING INSULIN PRODUCTION

For years, researchers thought it was impossible to restore the body’s ability to produce insulin. The reason? They thought that T1D completely destroyed the beta cells that produce insulin. BRI scientists helped change that assumption by showing that many people with longstanding T1D have “sleeping beta cells” that make a hormone called pro-insulin.

Normally, beta cells chop up pro-insulin to turn it into usable insulin. But sleeping beta cells have lost their molecular scissors.

Kayleigh and Merry don’t let type 1 diabetes get in the way of leading happy, active lives.

Dr. Greenbaum is leading the first study — called the Waking Up Beta Cells Study — of a drug that could kickstart these sleeping cells so they make full-fledged insulin. Merry was among the first patients in this study, which is only available at BRI and at the Rocky Mountain Diabetes and Osteoporosis Center in Idaho.

“I thought my chance at being part of research on a new therapy was dead and gone,” Merry says. “It’s incredibly exciting to know that BRI is creating hope even for people like me, after decades of living with this disease.”

HOPE FOR THE FUTURE

Today, Kayleigh is a high school sophomore who’s hatching plans to become a neonatal intensive care nurse.

“My experience with type 1 and BRI showed me how science and medicine can improve people’s lives, and helped me want to be part of something that’s larger than myself,” she says.

This sense of perspective might seem out of place in a 15-year-old — until you hear her mom talk about the family’s commitment to research.

“We might always live with type 1, but it will be a huge success if we can help researchers prevent it in other people,” Merry says. “This disease goes back five generations in my family and BRI gives me hope that even if my kids get it, my grandchildren won’t.”

To learn more about the Diabetes Clinical Research Program and to enroll in studies, visit BenaroyaResearch.org/diabetes-clinical-research
IMPROVING DIABETES RESEARCH WORLDWIDE

Type 1 diabetes (T1D) is an immensely complex disease, which means it’s going to take many minds — and many approaches — to conquer it. BRI plays a key role in this fight. Here are three ways we’re using our expertise to improve research worldwide.

A GLOBAL RESEARCH NETWORK

The Immune Tolerance Network (ITN) is a global consortium of top autoimmune disease researchers, collaborating to test new therapies. The ITN currently leads 70 clinical studies and is led by BRI’s former director, Jerry Nepom, MD, PhD. “Having the ITN here means BRI doesn’t just participate in the most important autoimmune disease studies — we help design and oversee them,” says Dr. Greenbaum.

The ITN’s studies encompass a range of autoimmune diseases and include a small number of T1D studies. For instance, Dr. Greenbaum and Dr. Buckner lead an ITN study investigating ways to extend insulin production in people with T1D. “This could help patients stay healthier and suffer fewer long-term consequences,” Dr. Buckner says.

SHARING SAMPLES WORLDWIDE

BRI has assembled one of the world’s largest collections of blood samples and medical information from people with T1D. To create this biorepository, we spent nearly two decades gathering samples from research volunteers and cataloging their health information.

Now researchers across the globe turn to us for samples. “A researcher might be studying a question that only relates to, say, a person who was diagnosed within five years,” says Cate Speake, PhD. “We send them samples so they can answer targeted questions that move research forward.”

ENSURING RESEARCH ACCURACY

As home to the JDRF Core for Clinical Assay Validation (CAV), BRI plays an important role in identifying T1D biomarkers and in helping outside researchers get the most accurate test results.

Biomarkers are substances in the blood that can suggest the presence of disease. The CAV is pinpointing key T1D biomarkers, such as markers that indicate which patients with T1D will keep making insulin for years and which patients won’t. This could help doctors anticipate a patient’s needs.

BRI is home to the JDRF Core for Clinical Assay Validation, which helps researchers get accurate test results at 24 research sites in eight countries.

The CAV also helps maintain quality control for a worldwide network of research labs by asking them to perform specific tests and reviewing their results. “If their results aren’t quite right, we help troubleshoot their testing process and find solutions,” Dr. Speake says.
In the past few years, Elisa Boden, MD, has seen more and more patients with celiac disease. The disease strikes when the immune system mistakes gluten — a mixture of proteins found in wheat and other grains — as an enemy and attacks the small intestine. This can trigger everything from chronic diarrhea to joint pain, and can increase the risk of serious health issues like cancer and weakened bones.

“The good news is, a gluten-free diet can eliminate many symptoms,” Dr. Boden says. “But we don’t know why the immune system malfunctions and we don’t have any other good therapies.”

Fortunately, Dr. Boden and BRI’s Bill Kwok hope to find biomarkers that indicate a person has celiac disease even when the disease isn’t active.

“This could lead to a new diagnostic test, which would be exciting because I really dislike telling patients they have to start eating gluten again,” Dr. Boden says.

For Dr. Boden, the studies are the latest step in her mission to solve the riddles of autoimmune disease in the digestive system.

“I hate seeing patients in pain,” Dr. Boden says, “and my goal is to keep using research to make progress until, hopefully, we find better therapies or even cures.”
THE BODY LIVES ITS UNDOING
is a reflection in poetry and visual art about autoimmune diseases and their impact on people.

A collaboration featuring poet Suzanne Edison, BRI researchers and artists, and doctors and patients, this book is a work of art that explores the world of autoimmunity.

Please join us to share in poetry readings, artist perspectives and group conversation around the autoimmune disease experience.

Dec. 4 7:00 – 8:30 pm
Science in the City Event, Pacific Science Center, Seattle

March 27 7:30 – 9:00 pm
Town Hall Seattle

THANK YOU!
Our 2018 Illuminations Luncheon attracted a record number of attendees — and raised more dollars than ever before! We also recruited more volunteers to the biorepository than ever before! We’re grateful to all attendees, donors and sponsors. Thank you for supporting BRI’s breakthrough research.

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