Pioneering research on peanut allergies at Benaroya Research Institute at Virginia Mason (BRI) was recently fueled with a $5 million grant from the National Institutes of Health to accelerate discovery of treatments. The research will explore how to match therapies to patients. Erik Wambre, PhD, and William Kwok, PhD, are the co-principal investigators for the studies, with Peter Linsley, PhD, serving as project leader for Gene Expression and Systems Immunology.

The project is a collaboration involving three BRI labs, Virginia Mason physicians and sponsors of two clinical trials that are continents apart. The researchers are hoping to discover more efficient and safer treatment options for peanut allergies than are currently available. “Ultimately, this study has the potential to truly upend the way we look at food allergy diagnosis and treatment,” says Jane Buckner, MD, President of Benaroya Research Institute.

The two-pronged study will first research peanut allergy patients’ immune responses and classify them into subgroups. Secondly, researchers will evaluate treatment options being used in a pair of clinical trials to determine how specific treatments can be matched to specific patients to teach their immune systems to tolerate peanut protein.

MATCH THERAPY TO PATIENT

Researchers will utilize a unique approach in solving this puzzle. “Food allergy is a multifaceted disease with many subtypes. Instead of looking for new allergy immunotherapies, we want to know which therapy should be applied to which patient—that is precision medicine,” says Dr. Wambre. “Our goal is high efficacy, high safety. To reach this goal we want to identify an immune signature that can guide treatment decisions and ensure better patient care.”

In the first part of the study, Virginia Mason co-investigators Mary Farrington, MD, David Jeong, MD, and David Robinson, MD, provide blood samples from their patients at the Virginia Mason Allergy, Asthma and Immunology Clinic. Drs. Wambre

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TESTING A NEW MS THERAPY

Last winter, Elena Connors commuted over treacherous roads from Richland to Walla Walla for her job as a Russian language interpreter. She blamed the strenuous trips for her painful headaches and put off seeing a doctor until they were so distressful, her husband, Charlie, took her to the emergency room.

“I had a series of tests, and around midnight the doctor announced that I likely had multiple sclerosis [MS].” says Elena. “We were surprised. But looking back, I realize that my body was changing over time. Now I realize that the fatigue was due to MS.”

MS is an autoimmune disease in which the body’s immune system mistakenly attacks myelin, which surrounds and protects the nerve fibers in the brain and spinal cord. This results in symptoms such as numbness in the limbs, fatigue, dizziness, paralysis and loss of vision. Upon her diagnosis, a relative “suggested seeing one of the wonderful doctors at Virginia Mason and honestly, it was the best decision ever!” says Elena. Though dealing with the disease was difficult for her and her family, Elena kept a positive outlook. “It took me a couple of months to realize that in an active stage of MS, I couldn’t push myself very hard,” she notes. “I was taking a medicine which helped, but I couldn’t tolerate the side effects very well and it limited me from doing things.”

Elena’s family has been extremely helpful through her experience and supports her positive approach. Pictured from left, Elena’s husband, Charlie, son Ian, Elena, and son Peter.

Her physician, Virginia Mason neurologist and clinical researcher Lucas McCarthy, MD, informed her about a new research study that is testing a drug with potentially fewer side effects than Elena’s current medicine. “I was interested in helping get the new medicine approved to help me and to give other patients one more choice to lead a quality life,” says Elena. “If scientists can improve existing medications or develop better ones, I feel it’s important to be part of the research.

“I joined the trial and my family noticed my almost sudden improvement within a couple of weeks. I had more energy, a better mood and I’m in a better place overall. I look forward to my visits to Virginia Mason. My wonderful team includes Dr. McCarthy, Katherine Wilder and Evelyn Fox. I feel so confident discussing any issues with them.”

The goal of the study was to see if an experimental oral drug, similar to a currently available MS medication, Tecfidera, will be just as effective and with fewer side effects. “Tecfidera is very safe and effective for prevention of MS relapses, but it has significant gastrointestinal side effects that lead to its discontinuation in a fair number of patients,” says Dr. McCarthy, principal investigator for the study at Virginia Mason and Benaroya Research Institute at Virginia Mason. “We would like to find a drug as effective that is more tolerable.”

MORE DRUGS AVAILABLE

“There are now more than 15 FDA-approved medications for stabilizing MS, with more than eight approved just since 2010,” says Dr. McCarthy. “The field of MS treatment is rapidly evolving with more effective therapies, but some options also have more serious risks and side effects. Despite these advancements, there are still many more unmet needs in MS treatment.”

“Research helped me find a new possible long-term medication once it’s approved by the FDA,” says Elena. “I hope more people can consider clinical trials for new medications to make a difference in their lives. It’s great that VM and BRI can provide access to trial medications for lots of people!”

Find resources and the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog.

Multiple Sclerosis (MS) Medications

This graph shows the rapidly expanding landscape of FDA-approved medications for preventing MS relapses and slowing disease progression. Green indicates Virginia Mason and Benaroya Research Institute participation in clinical research studies.
Children are helping Benaroya Research Institute scientists better understand immune system diseases. By taking blood samples from children without disease, researchers can compare their blood with the blood of children who have food allergies or type 1 diabetes.

The BRI Immune Mediated Diseases Biorepository is where these human blood, tissue and medical histories are located. While most participants are adults, BRI is now inviting children of all ages, who do not have an autoimmune disease, to donate a blood sample. Since 2000, more than 15,000 research participants have provided medical histories and donated more than 300,000 blood samples to support BRI scientists in their fight against diseases.

3 REASONS WHY KIDS ARE CRUCIAL

1. Kids Have Unique Diseases
BRI researchers are studying both food allergies and type 1 diabetes, which are mainly diagnosed in children. Samples from children help researchers understand how conditions that start in childhood develop. “In diabetes research, we are interested in what makes the immune system different in children and adults with diabetes compared to those without diabetes,” explains Cate Speake, PhD, BRI staff scientist.

2. The Immune System Changes
Since so many changes occur between birth and adulthood, it is important for BRI scientists to study the immune systems of children with and without disease. A young child’s immune system is typically less complicated than an adult’s. As children age, their immune systems are altered by the environment. For example, through exposure, a child’s body may develop allergic responses to harmless substances, such as cat dander, food and pollen. Also, an allergy that is present in childhood may be outgrown by the time the child reaches adulthood.

3. Kids Can Help
“Children might have a sibling with a peanut allergy or a friend with type 1 diabetes or they may not know anyone with a disease. All children can help sick kids by donating a blood sample to help move research forward,” explains Gina Marchesini, BRI’s translational research manager. BRI is dedicated to finding better treatments and cures for diseases, and science can only be conducted when both children and adults generously donate biological samples.

Find resources and the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog

HOW A TODDLER HELPS

Two-year-old Henry Achilles and his mom, Shannon, jumped at the chance to help advance immune system disease research at BRI—where Shannon works as a clinical financial analyst.

“We’re trying to do what we can to help accelerate progress against autoimmune diseases, especially since we have these diseases in our family,” Shannon says. “And we want Henry to grow up in a home that promotes science literacy.”

EMPOWERING VOLUNTEERS
Shannon was a little apprehensive on the day of Henry’s blood draw and came “armed and ready” with books and snacks. But she was immediately impressed with how BRI’s Clinical Research Center (CRC) staff made her and Henry comfortable.

During the draw, Henry sat on his mom’s lap while two nurses pinpointed where to insert the needle into a vein in his hand. Once the nurses found the spot, Shannon breathed easy while they quickly drew a small sample that was based on Henry’s weight, height and age.

When the draw ended, the CRC staff immediately gave Henry juice and crackers. He was smiling within 30 seconds of having the needle withdrawn. Then, when Henry got home, he asked about “the doctor” nonstop.

“We definitely made the right choice, but it wasn’t a decision we made lightly,” Shannon says. “Ultimately the knowledge of the impact his participation could have, coupled with Henry’s personality, made us want to give it a try. If it seems like a fit for you and your child, go for it!”

Henry Achilles is a research hero for donating blood to the BRI biorepository. His mom, Shannon, believes in helping accelerate progress against diseases.
upus is one of the most difficult autoimmune diseases to diagnose and treat. Clinicians and researchers at Virginia Mason and Benaroya Research Institute are leaders in looking for causes and cures of the disease. BRI Principal Investigator Adam Lacy-Hulbert, PhD, and his team recently made a new discovery regarding how lupus is triggered.

They also gratefully received a grant from The Marco J. Heidner Foundation to better understand how the newly discovered mechanism works and how to affect it.

Autoimmune diseases occur when the immune system—which is designed to protect the body against infection—makes a mistake and attacks its own healthy tissue. In lupus, the body attacks parts of dying cells throughout the entire body that would normally be quickly cleared away. This can cause inflammation and low blood cell counts, causing fatigue, joint pain, rash, chest pain, headache, confusion, bleeding problems and other symptoms ranging from mild to life-threatening.

NEW MECHANISM AT PLAY
Dr. Lacy-Hulbert and colleagues have identified a new mechanism that prevents the immune system from reacting to the debris that leaks from cells as they die. “We think that loss of this mechanism may be one of the reasons why some people develop lupus,” he explains. “We hope this grant will allow us to understand how this mechanism works in a particular type of immune cell, the plasmacytoid dendritic cell.” This cell can serve as a master regulator of immune responses and has been heavily implicated as a major contributor to lupus and other autoimmune diseases.

LUPUS AFFECTS 1.5 MILLION
Lupus affects 1.5 million Americans and is a chronic disease. It predominately affects women and usually develops between 15 and 46 years of age. There are very few effective long-term treatments and no cure.

“We hope our research will provide understanding into why certain people get lupus and will help in identifying new targets for drug development,” emphasized Dr. Lacy-Hulbert. “It’s very important to receive this pilot funding from The Marco J. Heidner Foundation. This is a compelling project that has a real possibility of generating new insights into disease. This grant gives us the opportunity to provide key data that shows our approach works and our innovative ideas are on track.”

FOUNDATION EMPHASIZES RESEARCH
“The Marco J. Heidner Foundation’s founder had a great interest in supporting medical research among other areas,” says Alison Yeager, managing director of Union Bank in Tacoma, which administers the foundation trust. “We chose to fund the Benaroya Research Institute grant because of the reputation of the organization, the impact on the community and the ability of the program to do good work with the support of the trust. We felt it was worthwhile for them to have a chance to succeed.”

“BRI is unique in having scientists that cover all stages of research, from basic research right through to clinical trials,” says Dr. Lacy-Hulbert. “We also have an amazing community of patients and volunteer research participants that provide blood samples for us to study disease. With this grant, we can take my basic research team and work more closely with other researchers who are experts in collaborating with patients and human samples. These interactions are essential for the sort of breakthroughs that are made at BRI. Ultimately, we hope this research can lead to better approaches to treatment.

“We all want to thank The Marco J. Heidner Foundation for their vital support, and we want to express our gratitude by using this wonderful opportunity they have given us to make important new advances in understanding lupus.”

Find more information on the Autoimmune Life blog: BenaroyaResearch.org/blog.
Researchers at Benaroya Research Institute and Seattle Children’s Research Institute are making key progress in their quest for an immunotherapy that cures type 1 diabetes once and for all.

Like all autoimmune diseases, type 1 diabetes strikes when immune cells turn against the body and attack it. The research team spent the past year and a half showing that it’s possible to isolate the cells that mount these attacks, and then “reprogram” them by editing their genes. The goal is to turn attacker cells into peacekeepers that stop type 1 diabetes in its tracks.

**NEW GRANT**

This innovative work was fueled by a $1 million grant from the Leona M. and Harry B. Helmsley Charitable Trust—which just rewarded the researchers with an additional $2 million to build on their progress and move closer to clinical trials.

“The idea behind immunotherapy is to insert instructions into immune cells that tell them to stop disease,” says BRI President Jane Buckner, MD. “This approach is already transforming cancer treatment, and we think we could do the same for autoimmune diseases.”

**EFFECTIVENESS OF TREATMENT**

According to Dr. Wambre, “The goal is to follow patients currently receiving treatment to look at the differences in immune response between groups of patients and understand how that response correlates with treatment effectiveness and side effects that the patients experience.”

What they discover could guide the design of a new strategy for immune intervention and provide a framework for applying precision medicine in peanut allergy. This study will also allow researchers to identify whether there are differences between children and adults receiving the same kind of therapy for peanut allergy.

“This will be the first demonstration that peanut allergy may no longer be considered a single entity with a ‘one size fits all’ approach to treatment,” states Dr. Linsley, who leads the data science core that serves as the bridge between the two parts of the study.

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**IMMUNOTHERAPY AIMS TO CURE TYPE 1 DIABETES**

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**CHANGE GENETIC INSTRUCTIONS**

This technology enables the researchers to change the genetic instructions inside the attacker T cells, transforming them into regulatory T cells that stop other cells from assaulting the pancreas.

“These engineered regulatory T cells, when returned to a person with diabetes, have the potential to stop effector T cells from destroying the body’s insulin-producing cells,” Dr. Rawlings says. “We believe this could be the key to curing type 1 diabetes.”

Find the full article on the Autoimmune Life blog: BenaroyaResearch.org/blog.
EVENTS

**LUPUS SYMPOSIUM**
What: A free educational event to learn the latest in lupus treatments and research as well as connect with others living with the disease. This event is open to all people living with lupus, their caregivers and healthcare professionals.
When: March 31, 1-4:30 p.m., Virginia Mason Medical Center, Lindeman Pavilion, Volney Richmond Auditorium, Level 1, 1201 Terry Ave., Seattle
Register: Learn more and sign up at lupus.org/pacificnorthwest.

**RESEARCH UPDATE EVENT**
What: An annual research update for all biorepository volunteers, their families and friends. At this event you will hear first-hand from BRI scientists about their current research, new discoveries and the progress being made against autoimmune disease and allergy.
When: April 21, 9 a.m.–noon. Refreshments served 8:30–9 a.m., BRI Auditorium
Register: Email biorepository@benaroyaresearch.org or call our toll-free line at 1-877-202-5200.