A new system model of multiple sclerosis (MS) that articulates more fully the many complexities of the disease was recently designed by Principal Investigator Estelle Bettelli, PhD, and her team at Benaroya Research Institute at Virginia Mason (BRI). Using the model, scientists can study the disease and how it progresses and look for better therapies and even ways to prevent disease. The model includes several groundbreaking features and studies a factor shown to have an important role in multiple sclerosis. Dr. Bettelli recently received a $2.1 million grant from the National Institutes of Health to further this research.

“We have discovered that the signal transducer and activator of transcription 1 (STAT1) gene, which is a key factor involved in immune system functions, can have a significant impact on multiple sclerosis in our system model,” says Dr. Bettelli. “When we eliminate STAT1, we seem to reduce destructive immune cells and even boost positive ones. This grant will allow us to explore further how STAT1 can be beneficial or detrimental depending on the targeted cell type. If we can learn more, in the future we could determine how to tweak the pathway in the right cell type to protect the cells in the central nervous system.”

**UNIQUE MODEL**

The new system model is unique in that it allows researchers to see what is happening in the central nervous system — the brain and the spinal cord — as well as the immune system. Scientists can also see in real time how this pathway affects cells in the brain and the immune system during disease progression. Several disease modifying therapies can modulate STAT1. Dr. Bettelli wants to investigate the mechanisms of STAT1’s protective effect during disease progression and determine how therapies might selectively impact cells in the immune system, the spinal cord and the brain. If some treatments have contrasting effects in the brain and the rest of the body, their efficacy might be more effective by targeting particular cells in the brain, she notes.

“Designing system models of disease is essential,” says Dr. Bettelli, “he others and therefore, we can narrow down on targets for human study. It isn’t a substitute for studying humans, but it points you in the right direction, with much more accuracy, in a timely way. What we do in system models can potentially lead to new translational and clinical studies that impact diagnosis and therapies.”

For more information visit BenaroyaResearch.org/MS.
Megan and Madeline Coder are 11-year-old identical twins who like to read and practice ballet. They live in Battle Ground, Wash., near the Oregon border. But during the last two years, they’ve boarded the train frequently to visit Seattle. They’re both participating in type 1 diabetes research studies at Benaroya Research Institute.

“Megan was 9 years old when I noticed her thirst and trips to the bathroom increasing,” says her mother, Keri Coder. “My sister was diagnosed with type 1 diabetes when she was 12, so I was aware of the symptoms. I hoped Megan had something else, but type 1 diabetes was the culprit. As a result, Megan’s nine siblings participated in the TrialNet screening to see if they had type 1 diabetes or were at risk. Madeline was the only one who had four of the five autoantibodies present. Her results qualified her to participate in the TrialNet Anti-CD3 Prevention Study.”

Type 1 diabetes is an autoimmune disease in which the body’s immune system makes proteins that attack and destroy the cells in the body that produce insulin. These proteins, called autoantibodies, can be found in the blood up to 10 years before someone is diagnosed with diabetes.

Led by BRI, Type 1 Diabetes TrialNet is an international network that conducts clinical studies aimed at preventing, delaying and reversing the progression of type 1 diabetes. In the TrialNet Anti-CD3 Prevention Study, researchers are studying whether a medication called teplizumab can help stop or slow down the destruction of insulin-producing cells in people at risk for type 1 diabetes.

HELPING OTHERS

“I want to help with this research to see if others, including me, can maybe be prevented from having diabetes,” says Madeline. “I hope diabetes can be both cured and prevented.” The study required Madeline to have infusions at BRI for 14 days in a row, with each visit lasting about four hours. She went to BRI five more times in the first year, and now she visits twice a year until the study is over or she develops type 1 diabetes.

Madeline’s twin sister, Megan, is participating in the BRIDge Study of Type 1 Diabetes. She is donating her blood and health information to help biorepository scientists understand how and why autoimmune diseases develop, identify how genetic risk factors influence the immune system to cause disease and develop targets for new therapies.

“I am very glad that both my sister and I have a chance to be there to help,” says Megan. “I hope that the research will find a way to prevent diabetes for my twin sister and many others that I don’t know. I want to thank BRI for doing this!”

Their mother, Keri, states, “My sister died in her early 30s from complications of type 1 diabetes, and my mom was diagnosed when she was 60 years old. We are hopeful that preventative and curative solutions can be found! We really love the staff at BRI. They are very kind, encouraging and supportive of the girls in their study and personal lives. We are all happy that we’ve participated.”

For more information visit BenaroyaResearch.org/diabetes-research.
"A lot of what we achieved in medical research at Benaroya Research Institute over the last 30 years we didn’t think was possible," says President Jane Buckner, MD. "Through new discoveries, including ones at BRI, we went from poor or zero treatments for autoimmune diseases to biologic medications that can rebalance the immune system. We saw people with rheumatoid arthritis or multiple sclerosis go from wheel chairs to walking and even running marathons! This dream was made into a reality by the many people who support us. They gave because they believed in us and had hope.

"Now we are looking toward a new vision where our knowledge of the immune system is harnessed to return people with incurable chronic diseases like type 1 diabetes, lupus, Crohn’s disease, ulcerative colitis, multiple sclerosis, rheumatoid arthritis, allergies and asthma back to health and ultimately to prevent these diseases from ever taking hold.”

Generous donors have enthusiastically stepped forward to make this new dream possible. They have endowed chairs at BRI to generate long-term funding to help secure the future of BRI. Over the past several months, more than $8.5 million has been committed, establishing four endowed chairs and partially funding a fifth chair, supporting BRI’s vision for the future.

“The endowed chairs provide vital and reliable funding for our leadership to attract and retain talented new faculty members, launch bold pilot projects and invest in innovative technology,” emphasizes Dr. Buckner. "We thank these generous supporters for their trust in BRI and their visionary hope in medical research to prevent and cure immune system diseases for millions of people and families.”

**LEONARD AND NORMA KLOORFINE BIOMEDICAL RESEARCH CHAIR**

“We believe in medical research and its ability to find cures for diseases,” say Leonard and Norma Kloorfine. “Human health is one of our main philanthropic drives. We want to support research that will help people today and future generations live longer and suffer less. We trust in Benaroya Research Institute and we’re pleased to provide a significant donation that will help sustain medical research.”

The Kloorfine’s gift funds a research chair to pioneer advanced immunology technologies and to design and implement insightful new experiments. This research takes advantage of the explosion of data from genome studies and molecular profiling to understand the functioning of the immune system in health and disease.

**GERALD NEPOM, MD, PHD, PRESIDENT’S CHAIR**

“I am supporting Benaroya Research Institute because I feel this is where the best research is being done,” says Rebecca Benaroya. "I am hoping I will live long enough to see a cure for type 1 diabetes. My whole family is so anxious for a discovery to help people with type 1 diabetes. Our grandson was diagnosed with the disease when he was 5 — and he is now 36 years old.”

Rebecca Benaroya’s gift funds a chair that provides annual funds for the BRI president to support important emerging research, invest in the latest technology and bring the best researchers to BRI. This fund is named in honor of Dr. Nepom, past director of the institute for 30 years. Jack Benaroya, a longtime donor to BRI with his wife Rebecca, passed away in 2012.
“So many of our dreams at first seem impossible, then they seem improbable, and then, when we summon the will, they soon become inevitable.”
– Christopher Reeve

**IMMUNOLOGY RESEARCH CHAIR**

“I’m very proud to have a long-time association with Benaroya Research Institute,” says George Weyerhaeuser. “It started very small and it has become an important institution with many valuable advances in medicine and research. BRI is an institution we can all be proud of and its strong leadership continues. I’m happy to give so it can continue to fight against autoimmune and other diseases. BRI deserves our support.”

George Weyerhaeuser’s gift helps establish an endowed chair, providing annual funds for the Immunology Research Program director to explore new avenues of immunology research, recruit innovative scientists and invest in state-of-the-art technology. This allows faster translation of discoveries from the lab to the clinic and back again.

**FRANK AND VIVIEN DVORAK DIABETES RESEARCH CHAIR**

“I’ve had diabetes for 55 years, I’ve been a patient at Virginia Mason for 50 years, and I’ve served a number of years on the BRI board,” says Frank Dvorak. “When the board discussed endowed chairs to help sustain BRI, Vivien and I wanted to contribute and lead by example. BRI is an extraordinary institution, with excellent scientists and staff and very successful research. It’s exciting to be a part of this great effort to help people who suffer with one or more of the 80+ autoimmune diseases.”

The Dvorak’s gift funds a chair providing annual support for the director of the Diabetes Research Program to recruit expert scientists, test new theories and provide bridge funding when needed. This will speed up efforts to achieve early diagnosis, better treatments, cures and prevention of type 1 diabetes.

**MARJORIE AND LEONARD WRIGHT TRANSLATIONAL RESEARCH CHAIR**

The estate of Leonard and Marjorie Wright of Mukilteo, Wash., supports the translational research chair. Marjorie Wright died in 2013 and Leonard Wright passed away in 2007. They both had been patients at Virginia Mason Medical Center. Translational research is a scientific approach that “translates” new laboratory discoveries into medical practices, using human samples to explore how the immune system is altered. Clinician findings are in turn shared with laboratory scientists to bring medical research full circle.

The Wright’s gift created an endowed chair that provides annual funds for the director of the Translational Research Program to acquire new technologies and dedicated researchers to accelerate scientific discoveries in this area of research. This provides the capacity to move quickly to test new hypotheses and pursue leads that are found in the laboratory.
HOW BRI FIGHTS MULTIPLE SCLEROSIS

LABORATORY RESEARCH
BRI lab researchers and colleagues discovered a subset of immune system cells which are believed to be potent inducers of MS and other autoimmune diseases. They are studying these cells to determine how to inhibit their harmful function. Researchers have also created models of the four different types of multiple sclerosis for study as well as the new model of MS with the key STAT1 factor.

TRANSLATIONAL RESEARCH
A recent discovery is potential novel biomarkers of MS that help identify disease activity and could serve as a target for new therapies. Also, BRI President Jane Buckner, MD, along with Virginia Mason Chief of Medicine and MS Clinical Research Director Mariko Kita, MD, and Joan Goverman, PhD, University of Washington, are studying samples of people with MS to understand those who have MS mostly in the spinal cord versus those with disease confined primarily to the brain. This research is being done through biorepositories of volunteers with MS providing blood samples and medical histories. For more information, visit BenaroyaResearch.org/MS-bio.

CLINICAL RESEARCH
BRI has five studies that are currently enrolling for different types of MS with a variety of medications and drug delivery systems such as oral medication, injections and infusions. One of the most promising new areas of research lies in remyelination — reversing damage and growing back nerves. BRI and Virginia Mason are now testing a new molecule for the first time in humans that has been shown to repair and reduce lesions. Learn more about clinical studies for multiple sclerosis at BenaroyaResearch.org/clin-neur.

WHAT IS MULTIPLE SCLEROSIS?
Multiple sclerosis (MS) is an autoimmune disease in which the body’s immune system mistakenly attacks the central nervous system, resulting in symptoms such as numbness in the limbs, fatigue, dizziness, paralysis and/or loss of vision. MS occurs when the immune system attacks myelin — the fatty substance that surrounds and insulates the nerve fibers in the central nervous system. Symptoms of MS will often improve and relapse with time and vary from one person to another. In progressive forms of multiple sclerosis, they gradually worsen. While there are a number of treatments for MS, there is no cure.

RESEARCH LEADS TO NEW MEDICAL GUIDELINES
A landmark research study to prevent the development of peanut allergy, from the Immune Tolerance Network (ITN), has led to new medical guidelines for health care providers. Benaroya Research Institute leads the ITN with BRI member and scientist Gerald Nepom, MD, PhD, serving as the director.

The guidelines, developed by an expert panel from the National Institutes of Health, were based on the groundbreaking Learning Early About Peanut (LEAP) study. The research showed that regular peanut consumption begun in infancy and continued until 5 years of age led to an 81 percent reduction in development of peanut allergy in infants deemed at high risk because they already had severe eczema, egg allergy or both. For more information, visit BenaroyaResearch.org/news.
WANTED: VOLUNTEERS OF ALL AGES

The BRI Control Biorepository is now recruiting volunteer participants of all ages (1-year-old and older) without autoimmune diseases. Volunteers answer health questions and donate a blood sample. Researchers use the samples to compare similarities and differences of healthy immune systems to ones with disease and identify biomarkers that are associated with the progression of disease.

If you, family members or friends are interested in supporting research and joining the BRI Control Biorepository, please contact Kassidy Benoscek, Clinical Research Coordinator, at 1-877-202-5200 or Control@BenaroyaResearch.org or visit BenaroyaResearch.org/healthy-control.

JOIN OUR ONLINE COMMUNITY

This spring, BRI is launching a blog with content dedicated to autoimmune diseases and allergies for people who have a connection and interest in these diseases. The blog will allow readers to share stories and engage with other community members. Timely stories and information will be regularly posted discussing what it’s like to live with these chronic diseases, latest news in this field and updates on BRI’s research and the people behind the research. Sign up for our e-newsletter and we’ll let you know when the blog is live. Visit BenaroyaResearch.org/signup.