Millions of Americans have diabetes and 5-10 percent of those have type 1 diabetes. Type 1 diabetes, once called juvenile diabetes, usually occurs in children or young adults. It is a lifelong autoimmune disease in which the body’s immune system attacks and destroys the beta cells in the pancreas that make insulin.

People with type 1 diabetes must inject themselves daily with insulin in order to stay alive. They must carefully monitor their blood sugar, and also balance their food intake and exercise. Long-term complications of type 1 diabetes include disabling or even life-threatening organ damage, including heart disease, kidney disease, blindness and nerve damage.

Benaroya Research Institute at Virginia Mason (BRI) is looking for ways to prevent, reverse and intervene in the disease at all stages. People with type 1 diabetes in their families can participate in studies at BRI including:

- A test for family members to see if they have the markers that show they are at high risk for type 1 diabetes. Relatives of people with type 1 diabetes have about a 3-4 percent chance of testing positive for autoantibodies associated with diabetes, about 15 times the risk of the general population.

- If a family member’s test results show these autoantibody markers, additional tests will be offered to estimate the chance of developing the disease. If family members qualify, they may have an opportunity to enroll in a prevention trial or close monitoring.

- People who have just been diagnosed with type 1 diabetes can seek enrollment in trials that are aimed at helping people make their own insulin as long as possible.

- Those with long-term diabetes can donate blood samples that allow scientists to understand the disease process.

Meanwhile, scientists are looking for ways to understand the cellular and molecular workings of type 1 diabetes to find ways to shut down or reverse this disease.

Benaroya Research Institute is an international leader in type 1 diabetes research and has investigated it for more than 30 years, starting with identification of a genetic marker for the disease. Exciting achievements over this time period have led

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Originally from Auburn, Wash., Kerri Arceo moved to Guam where she met her husband, a native of the island territory. For years she enjoyed a fulfilling life teaching religion at the St. John’s Episcopal School. That all changed one morning in 1995 when Kerri awoke thinking she had suffered a stroke.

“I was numb down the left side of my body — through my arm and leg,” Kerri says. Concerned but undeterred, she went on to school. “At one point I was walking down the hallway when my left shoe fell off. I didn’t even notice until a young student yelled out to me.”

Kerri went to the emergency room at the local hospital. When the attending physician didn’t know what to do, he advised Kerri to go off-island for further testing. At Valley Medical Center, in Renton, Wash., Kerri underwent an MRI procedure that showed lesions on her brain and was diagnosed with multiple sclerosis (MS).

Kerri soon found herself managing her new disease. This included countless hours of research, even bringing articles to discuss with her internal medicine doctor. “I actually contributed information to my doctor about Avonex,” Kerri remembers. “We got it shipped to Guam for me to try.”

Overpowered by worsening symptoms and the oppressive tropical heat, Kerri and her husband returned to Seattle. Here, the self-described “research junkie” became interested in clinical research, which ultimately led her to Benaroya Research Institute. For the past year, Kerri has been participating in a clinical study for fingolimod, the first oral immunotherapy treatment for MS. Today, Kerri is feeling her best in years. And she is grateful for the comprehensive care she receives as a participant in the study, led by Mariko Kita, MD, BRI Clinical Researcher and Director, Virginia Mason Multiple Sclerosis Center.

“I’d do anything to help,” she emphasizes. “But I don’t have money to donate to the cause, so I do research. I feel I’m helping so many people just by making myself available.”

To learn more about clinical research in multiple sclerosis, visit BenaroyaResearch.org/our-research.

Itn Completes Landmark Study

Early Consumption of Peanuts Prevents Peanut Allergy in High-Risk Infants

A new study recently reported in the New England Journal of Medicine demonstrates that consumption of a peanut-containing snack by infants who are at high-risk for developing peanut allergy prevents the subsequent development of allergy. The Learning Early About Peanut (LEAP) study, designed and conducted by the Immune Tolerance Network (ITN), with additional support from Food Allergy Research & Education (FARE), and led by Professor Gideon Lack at Kings College London, is the first randomized trial to prevent food allergy in a large cohort of high-risk infants.

The prevalence of peanut allergy has doubled over the past 10 years in the U.S. and numerous other countries. Peanut allergy, which now affects approximately 1.5 percent of young children, can cause adverse reactions ranging from development of hives and abdominal pain to severe anaphylaxis that requires immediate treatment with epinephrine.

Because of the risk of anaphylaxis, children with a peanut allergy are advised to avoid peanuts in their diet and must carry an epinephrine autoinjector kit with them for use in event of a severe reaction.

Peanut allergy is a negative response by the body’s immune system to harmless peanut proteins in the diet. This study was based on a hypothesis that regular eating of peanut-containing products, when started during infancy, will elicit a protective immune response instead of an allergic immune reaction. The study found in high-risk infants, sustained consumption of peanuts beginning in the first 11 months of life was highly effective in preventing the development of peanut allergy.

BRI leads the Immune Tolerance Network. For more information on this research study, visit BenaroyaResearch.org/news.
PREVENTION

Family members of someone with type 1 diabetes have 15 times the chance of developing the disease relative to the general population. A simple blood test for these relatives may detect autoantibodies that show an increased risk years before symptoms appear. Family members may be tested at no cost through a study called TrialNet Pathway to Prevention. Researchers will closely monitor participants identified to be at risk to help in early diagnosis and management of the disease. People at risk may be eligible to enter a prevention trial. Currently, three therapies are being tested to see if they can stop or slow down the immune system reaction that destroys insulin-making cells.

INTERVENTION AND REVERSAL

Studies through TrialNet and the Immune Tolerance Network (ITN) are looking at how to extend people’s ability to produce insulin when they are newly diagnosed with type 1 diabetes. Researchers have found at the time of diagnosis that many people continue to produce small amounts of insulin. Since even small amounts of natural insulin production can decrease the long-term effects of diabetes and improve short-term clinical management, scientists search for ways to keep these remaining cells producing insulin. Researchers are also launching studies for patients with longer-term diabetes and investigating an artificial pancreas to help people better manage their disease.

BIOBANKS

BRI uses biobanks to better understand biomarkers associated with the progression of type 1 diabetes and to identify targets for new therapies. A biobank consists of blood and tissue samples linked to medical and demographic information collected from people with a specific disease or condition. BRI maintains one of the world’s most robust biobanks for the study of autoimmune disorders including type 1 diabetes. BRI also manages several international biobanks for type 1 diabetes and shares information with scientists internationally to accelerate discoveries.

PERSONALIZED MEDICINE

In clinical trials, not all individuals respond in the same way to particular immunological therapies. In the laboratory, BRI scientists are investigating the molecular mechanisms of the type 1 diabetes autoimmune response, and of immune interactions with each therapy, to better understand disease progression and uncover new approaches to treatment. These studies also are developing methods to better predict a person’s disease risk and provide earlier diagnoses so that patients can begin treatments sooner, at a time when more beta cells remain and more of the insulin production function can be saved. Teams of BRI investigators, led by Alice Long, PhD, and Peter Linsley, PhD, are developing “discovery pipelines” for analysis of clinical trial samples to better understand the way different individuals respond to different therapies. This information is a cornerstone for tailoring therapy specifically to individuals — the right treatment for the right person at the right time.

To learn more about risk testing, joining a biobank and clinical trials, please call 800-888-4187 or visit BenaroyaResearch.org/our-research.

Staff at the BRI Diabetes Research Program include physicians, researchers, nurses, diabetes educators, program coordinators and administrative support. They are dedicated to finding causes and cures for type 1 diabetes.
What she's done for medical science, the arts and education is outright phenomenal,” says Tom Wight, PhD, Director of Benaroya Research Institute’s Matrix Biology Program. He’s talking about his grade school friend Ann Ramsay-Jenkins. They were good friends growing up together in Portland, Maine, but lost track of each other after high school.

Ann graduated from Skidmore College with a bachelor’s degree in public health administration and eventually was selected as a White House Fellow, and assigned to the Special Action Office of Drug Abuse Prevention in the White House. She served in the Office of Management & Budget, Executive Office of the President, and as director of the Office of Budgets at Harvard University. She was a director of Indian Heads Bank and assistant general manager of a public television station in New Hampshire and held a variety of other positions.

RENEWING A FRIENDSHIP

Eventually she made her way to the Northwest and served on the boards of many organizations. It was while she was chairing the board of UW Medicine that she saw a photo of her friend Dr. Wight in the lobby. As a professor of pathology at UW, he was a featured speaker at an upcoming lecture. When Ann called his office, their friendship was renewed. She recently asked Dr. Wight for a tour of his lab at BRI.

“The significance of his research is enormously impressive so I wanted to support his work,” says Ann. “I think it’s vitally important to push discoveries forward and encourage people to give to these cutting-edge endeavors.” With a $300,000 gift, Ann created the Ann Ramsay-Jenkins and William M. Jenkins Fellowship for Matrix Biology.

“We will use the generous fellowship to ensure bright young scientists with great potential can have an opportunity for support while they begin their research careers,” says Dr. Wight. “It is very difficult to get grant funding right away and this fellowship will help us keep talented young people. This is a tremendous boost to our program and will help accelerate our research. We greatly appreciate Ann’s gift.”

Dr. Wight directs the Matrix Biology Program and is grateful for the Ann Ramsay-Jenkins gift that will accelerate research.

The Matrix Biology Program at BRI focuses on the extracellular matrix, which is the material surrounding cells. Scientists are working to develop therapeutics to treat diseases based on regulating the impact of extracellular matrix on disease progression. The extracellular matrix contributes to heart and blood vessel diseases, cancer and diseases of the immune system such as type 1 diabetes.

SUPPORTING SCIENCE

Ann is thrilled with the opportunity to support this science. She also supports education and co-founded the College Success Foundation, which has helped 4,000 students achieve bachelor’s degrees. She has chaired the United Way of King County Board. In the arts, she has served as the chair of the Seattle Repertory Theatre and a board member of the 5th Avenue Theatre. Recently she even became a producer of a successful Broadway play, “First Date.”

“It’s great to see something you care about come to fruition,” says Ann. Benaroya Research Institute is grateful that Ann cares so much about the community, including medical research.

To learn more about contributing to BRI’s research, please visit BenaroyaResearch.org/support-us.
What are biomarkers, why does BRI work to discover them, and why are they important?

In my lab, we are trying to use biomarkers to better understand autoimmune diseases, particularly type 1 diabetes, and to try and use biomarkers to conduct smarter clinical trials. A biomarker is simply something you can readily measure, often in the blood, which tells you about what is going on in the body. Circulating c-peptide, for instance, is a biomarker of the ability to make insulin. The use of c-peptide as a clinical trial end point, championed by BRI’s Dr. Greenbaum and others, really revolutionized the testing of new therapies in type 1 diabetes.

There is still a long way to go to understand type 1 diabetes, especially in the ways in which disease varies between individuals. It is clear that disease progresses at different rates in different people, so it doesn’t make much sense to take a one-size-fits-all approach to treatment. Unfortunately, we don’t yet have a way to predict these outcomes.

Through a JDRF-funded consortium called the Biomarker Working Group, we are using new biomarker assays emerging from labs all over the world to try and solve this problem.

Our biomarker efforts at the BRI are certainly not limited to type 1 diabetes. My colleagues in the Translational Research and Systems Immunology programs are also trying to understand patient heterogeneity, to define relationships between genes and disease, and to predict positive responses to treatment in rheumatoid arthritis, multiple sclerosis, lupus and allergy. We are not the only institute doing this kind of research, but at BRI, we are making sure we take the hard next step — to translate them into real-world clinical use to really impact people with immune diseases.

BRI LEADS:

• **TrialNet**: In 2014, BRI became the TrialNet Hub and in June 2015, Carla Greenbaum, MD, BRI Director of the Diabetes Research Program, will become chair of the TrialNet network, supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health (NIH). The network includes 21 clinical centers working in cooperation with more than 200 screening and clinical research sites throughout the U.S. and seven other countries. TrialNet is dedicated to the study, prevention and early treatment of type 1 diabetes. Clinical trials have identified markers for risk and disease progression in diabetes and are testing therapies to intervene prior to onset of clinical symptoms, by blocking the immune attack on pancreatic beta cells that produce insulin.

• **TID Exchange Living Biobank**: BRI leads the operations center for the TID Exchange Living Biobank. By centralizing thousands of biological samples — together with clinical, demographic and study-derived information — the TID Exchange Biobank aims to be a world-class resource for innovative “real-time” clinical research, and a catalyst for exchange of knowledge and collaboration.

• **JDRF CAV**: The JDRF Core for Assay Validation (CAV) is located at BRI where scientists are working to isolate type 1 diabetes biomarkers. These will be used to identify people at risk for the disease, predict progression rates and assess how well treatments are working. The CAV is a hub for numerous projects throughout the international biomarker research community.

• **Immune Tolerance Network**: BRI leads the Immune Tolerance Network (ITN), a large international clinical research consortium supported by the National Institute of Allergy and Infectious Diseases of the NIH, conducting clinical trials and studies in transplantation, allergy and autoimmunity. The Network’s aim is to reprogram the immune system so that disease-causing immune responses are stopped while maintaining the immune system’s ability to combat infection. For type 1 diabetes, the ITN conducts clinical and pre-clinical studies designed to extend people’s ability to produce insulin when they are newly diagnosed with type 1 diabetes by rescuing beta cells from immunological attack.
TOUR BRI ON SCIENCE FRIDAYS
What: Attend our Science Friday Tour to learn more about BRI and autoimmune diseases research. The event includes a light breakfast, conversation with a leading researcher and a lab tour led by scientists.
When: 8–9:30 a.m., March 27, May 29, Sept. 25 and Dec. 4.
Register: Rachel Martin at 206-342-6519 or RMartin@BenaroyaResearch.org.

JOIN US FOR WALK MS
What: We’re participating in Walk MS and hope you are too! It’s the 25th anniversary of the walk to support people with multiple sclerosis and to fight the disease.
When: April 12 at the University of Washington, Seattle.
Contact: For more information visit nationalmssociety.org/Get-Involved.

SAVE THE DATE: BOEING CLASSIC GOLF TOURNAMENT
What: The Boeing Classic Golf Tournament, an official PGA Champions Tour event featuring the legends of golf 50 years or older, will benefit Benaroya Research Institute.
When: Aug. 17-23 at TPC Snoqualmie Ridge.
Contact: For more information and ticket options, please visit BoeingClassic.com.