One of the nation’s greatest research treasures was developed at Benaroya Research Institute at Virginia Mason (BRI) and is being enhanced every day. The treasure is more than 100,000 blood and tissue samples contained within huge freezers. They are a gift from volunteer donors with and without disease.

“In 2000, the leadership at BRI committed to the development of biorepositories in the area of diabetes and other autoimmune diseases, long before they were considered essential tools for research,” says Jane Buckner, MD, associate director of BRI and director of the Translational Research Program. “Today, we are unique in having such a rich and broad group of biorepositories for our research. We use them in a variety of ways that allow us to translate research from the laboratory to the patients and back again. This is at the very heart of our research today — moving what we learn in the labs into what we know about human diseases from our biorepositories and then using that information to set up clinical trials.”

DATABASE DEVELOPMENT

The motivation for forming the biorepository was to supply geneticists and immunologists with samples for their research. A database was set up to capture the information, says Carla Greenbaum, MD, BRI director of the Diabetes Research Program, who set up the first biorepository on diabetes. Each participant was interviewed to develop a “family tree” of autoimmunity. They were asked to have their family members donate blood samples as well to look for genes that may be causing autoimmune diseases and other biomarkers that are associated with disease. BRI has followed participants for several years, taking multiple samples to test in the labs.

Continued on page 5
Last December, Sonja Coomes began feeling pain and numbness in her left side. She visited her physician who couldn’t determine her illness and told her to call if it got worse. When her symptoms continued, she was sent to the emergency room at Harborview Medical Center. After numerous tests including an MRI, she was diagnosed with multiple sclerosis (MS) six months later.

“I was scared,” says Sonja. “I was diagnosed a week before my 21st birthday and I felt too young to deal with this. It wasn’t a good birthday present.”

A neighbor with MS referred Sonja to her doctor, Scott Nielsen, MD, a Virginia Mason Medical Center specialist in neurology and MS. “I talked with him about my different options for treatment,” says Sonja. “I decided to enroll in a BRI clinical research study for MS and also joined the BRI MS biorepository to contribute blood samples to help with research.”

Sonja is very enthusiastic about supporting research. “I want to do anything I can to help be part of a cure one day,” she says. “I hope the scientists can use my information to find better treatments and reduce symptoms for everyone with MS so we can live as normal a life as possible. I participate so scientists can keep finding answers to this disease.”

STUDY AIMS TO HALT DISEASE

Sonja joined a clinical research trial called STRIVE. The study’s goal is to determine how effective the drug natalizumab is at keeping patients who are in the early stages of relapsing-remitting multiple sclerosis free of disease.

“We hope to identify participants receiving natalizumab who experience a ‘permanent remission’ of their MS,” says Dr. Nielsen, BRI principal investigator of the study. “We want to determine which people respond to the drug by having no more clinical attacks, no new MS scars on the MRI scan and no increase in functional disability. This is important for our patients since we do not currently have an FDA-approved therapy that reverses damage already done by MS. However, we can alter the disease course early and try to prevent damage to the nervous system moving forward — and in the case of patients like Sonja with new MS, we hope to prevent the damage before it can occur.”

Sonja Coomes (right) enjoys time with her mother, Paula Markus. “My mom keeps me positive, helps me deal with the disease and is my best friend,” says Sonja.

“I just found out before the study that I have two more lesions on my brain,” says Sonja. “I feel positive that this drug will do its job and reduce my symptoms and lesions. The worse part of this disease for me is the fatigue, so I hope the drug will help with that too.”

Sonja still enjoys being outdoors and hiking. She is attending school to become a medical assistant and aims to obtain a nursing degree and specialize in neurology. “I’d like to advocate for people with this disease and help educate them.” And she’ll continue to contribute to research. “I’m excited to give in a way that directly advances knowledge about MS,” she says.

To find out more about MS clinical trials and biorepositories, visit BenaroyaResearch.org.
NEW TEAM – NEW HOPE

CONQUERING IBD

The incidence of inflammatory bowel disease (IBD) is growing, affecting greater numbers of people in more countries worldwide. Inflammatory bowel disease includes Crohn’s disease and ulcerative colitis. They are autoimmune diseases in which the body’s immune system attacks the intestines, resulting in intestinal inflammation, abdominal pain and bleeding.

IBD affects approximately 1.4 million Americans, with Washington State having one of the highest rates. This disease usually appears in young people, leading to many years of suffering and disability. Benaroya Research Institute is fighting this disease with more resources than ever. Scientists devoted to understanding and finding solutions to the disease are asking these questions:

• What causes the disease and how do people get it?
• Which genes play a role?
• How can we turn off the triggers that cause this disease?
• Why do medications for IBD work in some people, but not in others?
• How can we tailor our medications to find the best drug for our patients?
• How can we make our medications even better and less expensive?
• How can we prevent or cure this disease?

The team of scientists at BRI fighting against this disease include James Lord, MD, PhD, Elisa Boden, MD, and new to the team is Adam Lacy-Hulbert, PhD, and his laboratory (see box). The group is also supported by the Digestive Disease Institute (DDI) at Virginia Mason Medical Center, where Drs. Lord and Boden see patients with IBD in a center of excellence headed by Michael Chiorean, MD. Dr. Lord is also collaborating with a leading pharmaceutical company to find new immune therapies that could be developed and brought to patients as soon as possible.

With a dedicated focus on collaboration, these scientists investigate IBD at the cellular level, study patients with IBD in a biorepository containing blood and tissue samples, and apply discoveries with patients in innovative clinical trials. Many other BRI researchers also support this work. For more information about joining a biorepository or clinical trial, visit BenaroyaResearch.org.

UNDERSTANDING THE BASICS

LACY-HULBERT LAB LOOKS FOR ANSWERS

BRI Associate Investigator Adam Lacy-Hulbert, PhD, and his team of researchers, including Affiliate Investigator Lynda Stuart, MD, PhD, recently joined BRI. They bring new expertise in IBD and the basic functioning of the immune system. Dr. Lacy-Hulbert was previously assistant professor at Harvard Medical School and director, Program of Developmental Immunology at Massachusetts General Hospital.

“The last five years in IBD research have been very exciting,” says Dr. Lacy-Hulbert. “We have a much better idea about the genetic pathways for IBD. We are now pushing our laboratory work into understanding the roadmap in human disease. BRI is very forward thinking and brings a wide-range of expertise to bear on this work. I’m thrilled to collaborate with these scientists.”

Dr. Lacy-Hulbert’s team is studying one of the first responders in the immune system response called dendritic cells. He and his colleagues have identified a gene that these cells use to educate the immune system in responding to intestinal bacteria. These studies will provide a better understanding of how the immune system works in IBD and may identify ways to manipulate this gene to reduce the harmful immune response in patients with IBD.
Robert Vernon, PhD, a research associate member at BRI, and his team are pioneers in the development of engineered replacements for tissues and organs lost through disease or trauma. Two projects, which have important implications for persons suffering from type 1 diabetes or vascular disease, are part of what drew Leonard and Norma Klorfine and the Klorfine Foundation to Dr. Vernon’s work. When they saw the therapeutic potential of this research, they generously provided a grant to significantly accelerate these projects.

ISLET IMPLANT

One object is a quarter-inch diameter disk perforated with holes. The disk, which is made of a spongy biocompatible natural material, is part of a Bioengineered Islet Implant (BI). The BI, a device for transplantation of islets of Langerhans (the insulin-producing units of the pancreas), is designed to house donor islets within a controlled microenvironment that promotes islet survival, vascularization, and protection from immune attack by the recipient. The ultimate goal of the BI project is to develop an effective means of islet replacement therapy for people with type 1 diabetes whose islets are destroyed by their own immune system during the course of the disease. It is envisioned that BIs designed for human patients will be roughly the shape, size and thickness of a credit card and will be placed inside the peritoneal cavity or under the skin.

BLOOD VESSEL REPLACEMENT

The other project is represented by a white three-inch tube — a prototype of a tissue-engineered blood vessel (TEBV). Dr. Vernon and his team are developing TEBVs as blood vessel replacements that will function like human arteries. An important component of the research is focused on finding a way to induce the muscle cells that make up the walls of the TEBVs to produce the rubber-like protein elastin — a component of native blood vessels that provides flexibility and strength.

Donations from individuals and private foundations are vital to the advancement of BRI’s research efforts. About 20 percent of BRI’s research support is provided by nongovernmental sources. These private donations allow BRI researchers to start innovative pilot programs, purchase new equipment and support young investigators. For more information on donating to BRI, please visit BenaroyaResearch.org/support-us.

THANKS TO THE RASMUSON FOUNDATION FOR SUPPORTING ALASKANS

Benaroya Research Institute sincerely thanks the Rasmuson Foundation of Anchorage, Alaska, for providing a $1 million grant to bring education and access to clinical trials to Alaskans suffering from autoimmune diseases, cancer and many other conditions.

- The grant enrolled a total of 87 Alaskans into clinical trials.
- They joined more than 30 different clinical trials for diseases including type 1 diabetes, multiple sclerosis, rheumatoid arthritis, scleroderma, hepatitis and many types of cancer.
- Many of these patients graciously donated blood and tissue samples for the BRI biorepositories to help advance research.
- Alaskan study participants increased the understanding and treatment for a variety of diseases. For example, multiple Alaskans were enrolled onto a hepatitis C trial for a drug called Boceprevir. Based on this research, the drug has been approved by the FDA and is now the standard of care for treating hepatitis C.
- The grant provided participants with 431 round-trip visits to Seattle from Hoonah to Fairbanks and numerous cities in between.
- BRI and Virginia Mason staff provided health information to the state by talking with clinicians and attending health fairs and conferences.

Leonard and Norma Klorfine generously support tissue engineering projects led by the Vernon Laboratory.
**ASK THE RESEARCHER**

Q. Some of my relatives have type 1 diabetes. My husband and I have two children. Should we have them tested to find out if they will develop type 1? If so, at what age should they be screened?

A. Thank you for asking such an important question. Family members of someone with type 1 diabetes have a 15 times greater risk of developing diabetes than the general population. A simple blood test for these relatives may detect autoantibodies that show an increased risk years before symptoms appear.

Your children and other family members may be tested through the Type 1 Diabetes TrialNet study called Pathway to Prevention, at no cost. This includes people who are:

- 1 to 45 years old and have a brother, sister, child or parent with type 1 diabetes
- OR
- 1 to 20 years old and have a cousin, aunt, uncle, niece, nephew, half-brother, half-sister or grandparent with type 1 diabetes.

Children may be retested annually for risk until age 18. We recommend that children be screened at age 1 or as soon as possible after that, because the rate of type 1 diabetes is increasing fastest in children under 5 years of age. Researchers will closely monitor participants at risk, which will help in early diagnosis and management of the disease. Early control of diabetes may minimize the risk of future complications. Children found to be at risk may be eligible to enter a prevention trial as early as 3 years of age. Those who participate help move research forward to find ways to prevent type 1 diabetes.

- Benaroya Research Institute is the Northwest Coordinating Center for TrialNet.
- You can be tested here or we can arrange for testing anywhere in North America.
- To learn more, visit BenaroyaResearch.org/biorepositories or call toll-free 1-877-202-5200.

**CARLA GREENBAUM, MD**
**DIRECTOR, BRI DIABETES RESEARCH PROGRAM**
**DIABETES@BENAROYARESEARCH.ORG**

**BIOREPOSITORY**

A biorepository, or biobank, consists of blood and tissue samples linked to medical and demographic information collected from people with a specific disease or condition. All of the information gathered is kept confidential, and samples and health information used by scientists are coded with a number. BRI actively maintains 11 different biorepositories including one with healthy samples for comparison purposes.

“BRI uses the biorepositories to better understand the biomarkers associated with the progression of these diseases and identify targets for new therapies,” explains Dr. Buckner. “We also compare the samples donated by these research participants with samples from healthy volunteers to advance our understanding of how and why autoimmune and other diseases develop, and to identify how genetic risk factors for the diseases affect the immune system to cause disease.

“We collaborate with other researchers to use this information and also have collaborative agreements with pharmaceutical companies to integrate scientific discovery, the development of diagnostic and treatment solutions and their clinical application,” Dr. Buckner notes. “We anticipate that this will accelerate as never before our ability to better understand, diagnose and treat these illnesses.”

For information on participating in a biorepository or learning more, please visit BenaroyaResearch.org/biorepositories or call toll-free 1-877-202-5200.

**DID YOU KNOW?**

The incidence of type 1 diabetes is growing throughout the world. In the U.S., the disease is increasing 3–5 percent per year, especially in young people. The Nordic countries have one of the highest incidence of the disease and have been closely tracking it through their registry system.

![Incidence of diabetes in children under age 10 in Norway](image3.png)
IF YOU HAVE QUESTIONS FOR ASK THE RESEARCHER, PLEASE SEND THEM TO ASKTHERESEARCHER@BENAROYA.ORG.

Continued from front page

Autoimmune diseases happen when the body’s immune system attack healthy tissue — will explain the disease course and help answer your questions. BRI Director Gerald Nepom, MD, PhD.

What if medical research could combine mistakes by the immune system can cause different diseases, but also using this information to test new treatments. Autoimmune research has been leading causes of destructive diseases. People with autoimmune diseases are shared, exactly what Benaroya Research is doing. The scientists aren’t taking on all 80.

For more information, visit BenaroyaResearch.org or call 206-342-6500.

Contact:
Rachel Martin at (206) 342-6519 or RMartin@BenaroyaResearch.org.

2014 SCIENCE FRIDAY
What: Learn more about medical research through Science Friday events at Benaroya Research Institute that include a light breakfast, conversation with a leading researcher and a lab tour led by scientists.
When: From 8:00 a.m. to 9:30 a.m. on Jan. 24, March 14, May 9, July 11, Sept. 12 and Oct. 24.
Contact: Rachel Martin at (206) 342-6519 or RMartin@BenaroyaResearch.org.

GIVE TO BRI
What: Contributing to BRI as part of your end-of-year giving provides the Institute with vital funds to continue innovative research. Thank you for your generosity. Every gift, large or small, makes a difference.
Contact: Visit BenaroyaResearch.org/support-us or return the enclosed donor envelope.

GO GREEN WITH THE E-NEWSLETTER
What: Receive the electronic version of our newsletter.
Contact: Fill out the enclosed postcard or e-mail us at news@BenaroyaResearch.org.