Benaroya Research Institute at Virginia Mason (BRI) conducts numerous clinical research trials each year in many different diseases: through a Diabetes Research Program partnership with Seattle Children’s, the National Institutes of Health (NIH) Type 1 Diabetes TrialNet and the BRI Clinical Research Program with physicians at the Virginia Mason Medical Center. In addition, BRI is involved in trials with the Immune Tolerance Network (ITN), a research cooperative network, funded by the National Institute of Allergy and Infectious Diseases, part of the NIH. In 2011, BRI Director Gerald Nepom, MD, PhD, was named director of the ITN and earlier this year BRI was awarded a $27 million grant annually over the next seven years to provide management and oversight of the Network and fund the ITN’s development, coordination and implementation of international clinical trials for novel therapies in transplantation, allergy and autoimmune disease as well as implementation of mechanistic, laboratory-based studies. Currently, the ITN program has clinical and laboratory investigators conducting studies at 110 clinical sites in the U.S., Canada, Mexico and the United Kingdom.

The ITN program mission is to advance knowledge and develop clinical therapies that will direct the body’s immune response toward repairing tissue damage and reversing and preventing disease. The immune system plays a vital role in keeping our bodies healthy and protected from infection. However, autoimmune diseases such as type 1 diabetes, multiple sclerosis and lupus, among others, result when the immune system aberrantly attacks the body’s own cells. Allergies result when the immune system overreacts to a substance that is generally harmless. Following organ or tissue transplantation, the body’s immune system rejects the transplanted tissue, requiring the use of immunosuppressive drugs. In all of these examples, the ITN strategy is to reeducate the immune system to learn to stop this dangerous response, and to recognize the affected tissue as its own.

“The ITN program conducts game-changing clinical research studies that are unique,” says Dr. Nepom. “The aim is to achieve ‘immune tolerance’ which means that we are testing new therapies that will stop the immune system from attacking the body’s own tissues and redirect the immune system so it will tolerate its own tissues.”

The ITN grant is one of the largest NIH awards made to any institution and is a significant recognition of the stature of BRI in the research community. “Having the ITN as part of BRI makes perfect sense,” says Dr. Nepom. “The ITN’s philosophy and approach to...”

Continued on page 5
On July 5, 2013, Chris Wood became extremely ill from food poisoning he contracted at a Fourth of July picnic. But in addition to the normal, highly unpleasant symptoms, Chris’s joints were so swollen he could hardly stand, walk or write. Frightened and having no health insurance, Chris made his way to the Union Gospel Mission in Yakima, Wash., for treatment.

Chris’s doctor confirmed a salmonella infection, yet the cause of his joint inflammation was still unclear. For this, Chris was prescribed anti-inflammatory drugs and steroids that proved only minimally effective. A family friend then suggested that Chris be seen by her Virginia Mason Medical Center rheumatologist, Jeffrey Carlin, MD, who is also a BRI clinical investigator.

“Almost instantly, Dr. Carlin said I had axial spondyloarthritis,” Chris says. “Tests showed I have the gene indicated for this disease and that it was probably triggered by the salmonella infection.”

Spondyloarthritis (SpA) is an umbrella term for a group of immune-mediated rheumatic diseases. Some forms of this arthritis are associated with other autoimmune diseases such as inflammatory bowel disease, ankylosing spondylitis and psoriasis, and one type is triggered by an infection. It is not known what triggers the onset of the arthritis, but there does seem to be a genetic predisposition, associated with the gene HLA-B27, to develop these diseases. Symptoms include painful inflammation of the spine, sacroiliac joints and peripheral joints and pain and stiffness in the back, the neck, the back of the heel and underneath the foot.

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Fortunately for Chris, Dr. Carlin was conducting a clinical trial for axial SpA patients. Chris was quickly screened for and enrolled onto the study for which he now receives biweekly injections of a monoclonal antibody called adalimumab.

“The goal of this trial is to evaluate the effectiveness and safety of continuing adalimumab for maintaining remission in participants without X-ray evidence of spondyloarthritis,” says Dr. Carlin. “Adalimumab is already FDA approved for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn’s disease and ulcerative colitis. It cannot cure these diseases, but can control these disorders very effectively.”

“I’m so thankful for this trial,” says Chris. “Within about two weeks my symptoms were gone.”

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With his arthritis under control, Chris can now focus on starting his new career as an electrician while pursuing his favorite pastime: salmon and steelhead fishing.

“For me, the chance of having no arthritis is better than the possibility of maybe having some side effects. I’d really encourage people to be open-minded about clinical research.”

To find out more about rheumatology clinical trials, visit BenaroyaResearch.org.
NEW BIOREPOSITORY STUDIES CELIAC DISEASE

Celiac disease can be difficult to diagnose and has no cure. Benaroya Research Institute (BRI) recently launched a new biorepository for the disease to collect blood samples, tissue samples and medical histories of people with the disease. This will allow scientists to study the disease and research novel approaches to the diagnosis and treatment of celiac disease, says Elisa Boden, MD, clinical researcher at BRI who is establishing the Celiac Disease Biorepository. Dr. Boden is also a gastroenterologist at the Digestive Disease Institute at Virginia Mason Medical Center.

Elisa Boden, MD

Celiac disease occurs when the immune system attacks the small intestine after exposure to gluten (a protein found in wheat, rye and barley). This causes inflammation and damage to the small intestine, which can prevent the absorption of water and nutrients into the body. Celiac disease is also known as coeliac disease, celiac sprue, non-tropical sprue, and gluten sensitive enteropathy. Celiac disease is hereditary, meaning that it runs in families. About 1 in 10 people with a first-degree relative with celiac disease (parent, child, sibling) will develop celiac disease.

Celiac disease is estimated to affect 1 in 100 people in the United States and its incidence appears to be rising. In addition, 2.5 million Americans are undiagnosed and may be at risk for long-term health complications. Celiac disease can develop at any age, affecting both children and adults. Left untreated, celiac disease can lead to additional serious health problems. These include nutritional deficiencies, anemia, increased risk of infections, osteoporosis, dermatitis herpetiformis (an itchy skin rash), infertility or miscarriage, neurological conditions including seizures and migraines, and intestinal cancers.

GLUTEN-FREE DIET

Currently, the only treatment for celiac disease is lifelong adherence to a strict gluten-free diet. People living gluten-free must avoid foods with wheat, rye and barley, found in many foods including bread, pasta and beer. Gluten is additionally used commonly as a filler in many processed foods. With the increased marketing and development of gluten-free foods, a gluten-free diet has become easier to follow. However, many people with celiac disease still find the diet restrictive and difficult to follow, especially when eating outside their home. In addition, the majority of people with celiac disease continue to demonstrate evidence of ongoing intestinal damage even while attempting to adhere to a strict gluten-free diet. Thus, there is a clear need for adjunctive therapies in the treatment of celiac disease.

There are additionally some people who may have “gluten intolerance” without having celiac disease. These patients may experience symptoms of abdominal pain, bloating, diarrhea or fatigue when they eat a diet containing gluten. While these are common symptoms of celiac disease, these individuals do not have the characteristic small intestinal damage or tissue transglutaminase (tTG) antibodies found in celiac disease. “We do not yet clearly understand what causes non-celiac gluten intolerance,” says Dr. Boden. “Some experts have suggested that many of these patients have small intestinal damage, but have antibodies that are not found in people with celiac disease. These patients are at increased risk of gluten-related symptoms, but do not have the characteristic intestinal damage seen in people with celiac disease.”

SYMPTOMS OF CELIAC DISEASE

Celiac disease can be difficult to diagnose because it may affect many organ systems outside the intestines. Some people with celiac disease have no symptoms. However, all people with celiac disease are at risk for long-term complications, whether or not they display any symptoms.

DOES YOUR CHILD HAVE CELIAC DISEASE?

Digestive symptoms are more common in infants and children. Some of the most common symptoms found in children include abdominal pain and bloating, chronic diarrhea, vomiting, constipation, irritability and behavior issues, weight loss, fatigue and delayed growth.

DO YOU HAVE CELIAC DISEASE?

Adults are less likely to have digestive symptoms, with only one-third experiencing diarrhea. Adults are more likely to have symptoms such as unexplained iron deficiency, fatigue, bone or joint pain, arthritis, bone loss, depression or anxiety, tingling in hands and feet, seizures, migraines, infertility, canker sores and rashes. For more information, visit BenaroyaResearch.org.

JOINING THE CELIAC DISEASE BIOREPOSITORY

If you are interested in joining or learning more about the Celiac Disease Biorepository, please call Study Coordinator Kassidy Benoscek at (206) 342-6537 or toll-free at 1-877-202-5200 or via e-mail at kbenoscek@benaroyaresearch.org.

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“Celiac disease is restricted to people with certain HLA class II genes,” she explains. “About 40 percent of people have these genes but only 1 percent get the disease. This tells us there are other important genetic or environmental factors that play into the immune reaction in celiac disease. By studying people with celiac disease and healthy people with the same genes, we hope to discover both factors that trigger disease and also those that protect healthy people. We will use this information to develop ways to put the brakes on the immune system to stop it from reacting to gluten. Our hope is to find ways to eliminate the devastating symptoms of this disease and stop damage to the small intestine.”
The estate of Leonard and Majorie Wright of Mulkiteo, Wash., recently bequeathed $2.5 million to Benaroya Research Institute for translational research. Marjorie Wright died in 2013 and Leonard Wright passed away in 2007. They were both patients at Virginia Mason Medical Center.

“We are so grateful to the Wright family for this generous bequest. Planned gifts such as this allow us to achieve our long-term vision of conquering autoimmune diseases,” says BRI Director Gerald Nepom, MD, PhD. “We can acquire new technologies and dedicated researchers to accelerate scientific discoveries.”

The Wright bequest will be used for translational research at BRI. Translational research is a scientific approach that “translates” new laboratory discoveries quickly into medical practices. Clinician findings are in turn shared with laboratory scientists to bring medical research full circle. An important part of translational research is the biorepositories consisting of blood and serum samples and medical histories provided by volunteers. Researchers study them to better understand genetics and environmental factors in diseases and how to better diagnose and treat them.

INNOVATIVE TECHNOLOGY

“We plan to use the funds from the Wright bequest to support our efforts to better understand human autoimmune diseases by using cutting-edge technology in combination with our biorepository of samples,” says Jane Buckner, MD, BRI associate director and director of the BRI Translational Research Program. “Part of this bequest will be used to support the purchase of a state-of-the-art flow cytometer. This instrument has the capability to examine blood cells on an individual basis, telling us not only how many immune cells are present in the blood but also how they function and what their role is in the immune response against the body. This approach at BRI has already helped develop important insights into the causes of type 1 diabetes, rheumatoid arthritis, lupus and allergies. We hope to extend these studies to more diseases, and to more patient samples. In this way, we will be able to understand the diseases better, but also the differences between patients, their disease progression and response to therapy.”

The bequest will also be used to support scientists at BRI who are performing translational research. This gives them the capability to move quickly to test new hypotheses and pursue leads that are found in the laboratory. “This will accelerate our research,” says Dr. Buckner. “We greatly appreciate the foresight shown by the Wrights in making this gift possible.”

You can have a long-term impact on research at BRI by making an estate gift. Please contact the Virginia Mason Foundation for more information at (206) 583-6083 or e-mail foundation@vmmc.org.

U.S. CONGRESSMEN VISIT BRI

Benaroya Research Institute leadership provided Congressman Dave Reichert and Adam Smith with tours of the Institute. They discussed the latest research at BRI and the need for National Institutes of Health funding, especially in bringing scientific advances as quickly as possible to patients.

Karen Cerosaletti, PhD, and John Gebe, PhD, are scientists in the Translational Research Program that benefits from the Wright bequest.

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How do I find a doctor who specializes in autoimmune diseases? There is no medical specialty called “autoimmunity.”

Although the causes of autoimmune diseases are shared between diseases, the diseases themselves affect different parts of the body. Because of this, each autoimmune disease has traditionally been treated by the subspecialists that are experts in the part of the body or system that is affected by an individual disease. For example, a patient with weakness or numbness will see a neurologist, a patient with thyroid disease or diabetes will see an endocrinologist, someone with abdominal pain and diarrhea will see a gastroenterologist, patients with rashes such as psoriasis will see a dermatologist and someone with arthritis will see a rheumatologist.

This makes sense because these subspecialists are expert at diagnosing and caring for patients with these problems. However, once someone is diagnosed with an autoimmune disease, it may be helpful to find a physician within a subspecialty who is particularly interested and involved in the care of the autoimmune disease that you have. It is important to work with a physician who is comfortable with the treatment of these diseases and who is up-to-date on the most recent discoveries.

For example, a patient with multiple sclerosis (MS) may be diagnosed with the disease by a general neurologist then choose to see someone who has a strong interest in MS; this may also be the case if someone is diagnosed with Crohn’s disease or ulcerative colitis. In the case of rheumatology, many of the diseases seen by rheumatologists are autoimmune in nature, including diseases such as rheumatoid arthritis, systemic lupus, axial spondyloarthritis and many others. Most rheumatologists are expert in treating these autoimmune diseases and prepared to identify other autoimmune diseases as well.

If you have an autoimmune disease, it is important to keep all of your doctors informed about your diagnosis, treatments and any new symptoms or concerns that you have, so that they can provide you with the best possible care and advice.

JANE BUCKNER, MD
BRI ASSOCIATE DIRECTOR
TRANSLATIONAL RESEARCH PROGRAM DIRECTOR
RHEUMATOLOGIST, VIRGINIA MASON MEDICAL CENTER

JENNY BUCKNER, MD
BRI ASSOCIATE DIRECTOR
TRANSLATIONAL RESEARCH PROGRAM DIRECTOR
RHEUMATOLOGIST, VIRGINIA MASON MEDICAL CENTER

NEW THERAPIES
Continued from front page

science is similar to that of BRI and will help achieve our ultimate goal of improving people’s lives by finding the right therapy for the right person, at the right time. In addition to the leadership role for BRI, this award will provide more opportunities for BRI scientists to participate in cutting-edge therapeutic studies and increase the scope and impact of our research.”

The ITN program is also a leading innovator in clinical transparency, as well as data and sample sharing through TrialShare, an online resource that provides access to underlying data, analyses and samples from ITN’s clinical trials. The TrialShare web portal addresses a critical gap in data sharing, making information available from research studies to anyone, so that results from clinical trials are fully accessible to the public.

To learn more about BRI and the ITN, visit BenaroyaResearch.org.

DID YOU KNOW?

The risk of family members of someone with type 1 diabetes 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 through a study called TrialNet Pathway to Prevention at no cost.

• 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.

• To learn more visit TrialNet.org or call 1-800-888-4187.
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 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 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: If you’d like to receive the electronic version of our newsletter instead of the print newsletter, please e-mail us at news@BenaroyaResearch.org.