



BRI Takes New Lead in Autoimmune Disease Research

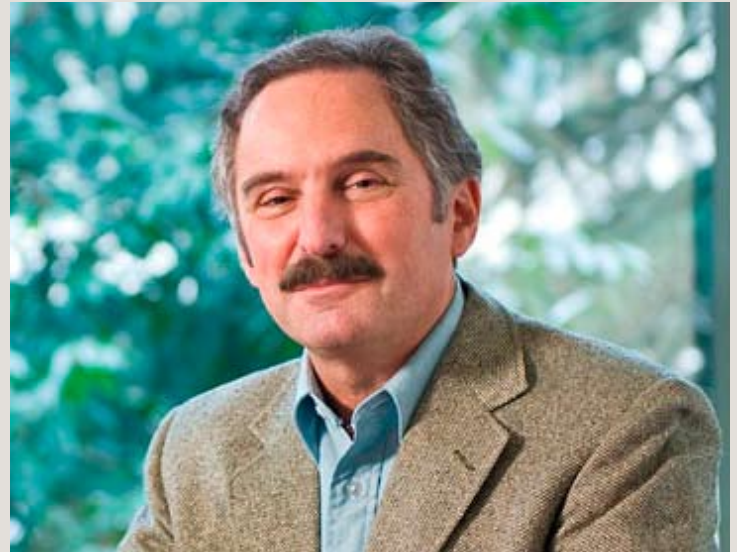
Benaroya Research Institute at Virginia Mason (BRI) is taking an even greater role as an international leader in immunology research. The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), has named BRI Director Gerald T. Nepom, MD, PhD, as the Director of the Immune Tolerance Network (ITN). As one of the largest government-funded clinical research networks in the country, the ITN works to establish new treatments for diseases of the immune system. Dr. Nepom will maintain his position with BRI in addition to his new role with ITN.

“This is an exciting time in autoimmune diseases research,” says Dr. Nepom. “We have a tremendous opportunity to link scientific advances with innovative clinical research efforts to treat autoimmune and immune-mediated diseases.”

The ITN, founded in 1999, currently operates at 200 clinical sites in more than 10 countries under a \$224 million NIAID contract in partnership with the Juvenile Diabetes Research Foundation (JDRF). The ITN conducts clinical trials of specialized immune tolerance therapies for the prevention of organ transplant rejection (in liver, kidney and islet transplantation); the treatment of autoimmune diseases (such as Type 1 diabetes, multiple sclerosis, lupus and others); and the prevention and treatment of allergies and asthma.

The ITN, with offices in San Francisco, Bethesda, Md., Pittsburgh, and now Seattle, is conducting or has completed 28 clinical research trials, many considered “first in humans” or “first of its kind” research. The consortium is led by a steering committee of some of the world’s foremost authorities on immune tolerance.

“I’m so pleased NIAID selected Dr. Nepom,” says Senator Patty Murray. “His leadership is invaluable to advancing science and eliminating autoimmune diseases that affect one in 20 Americans. Research in this field is so important to our families because more people in our community have autoimmune diseases.”



Gerald T. Nepom, MD, PhD, the Director of BRI, recently became Director of the Immune Tolerance Network as well. The two organizations have similar missions, to eliminate autoimmune and immune-mediated diseases. Dr. Nepom also recently received the Juvenile Diabetes Research Foundation International (JDRF) David Rumbough Award for Scientific Excellence, the highest honor of JDRF.

DID YOU KNOW?

Immune Tolerance Therapy

Autoimmune diseases occur when the body’s immune system mistakenly attacks its own healthy tissues. Many treatments for these diseases suppress the entire immune system. This can reduce symptoms of the disease, but it also suppresses the disease-fighting part of the immune system, leaving patients more vulnerable to viruses, bacteria and even certain types of cancer. In the new immune tolerance therapies, drugs target only the parts of the immune system that have gone awry. The goal is to stop the autoimmune disease while leaving the body’s disease fighting abilities intact. Both BRI and ITN are working on these pioneering treatments.

Tetramers — Path to a Cure

In the late 1990s, the National Institutes of Health (NIH) initiated a contest. The institute knew advancing medical research required a special scientific tool — a bioengineered biomarker. This biomarker would be able to latch onto specific blood cells so they could be researched. The biomarker would also track whether new molecular immunology treatments were working. “We needed to study one type of cell in a drop of blood that contained a million cells. It was like trying to find a needle in a haystack. We needed a really efficient ‘molecular magnet,’” says Gerald Nepom, MD, PhD, Director of BRI.

Several research institutions, including BRI, were each awarded small competitive grants to see if they could solve this puzzle. BRI’s scientific team, led by William Kwok, PhD, won the contest by creating a novel “tetramer,” a spider-like synthetic molecular biomarker with four flexible “arms” that can seek out and latch onto specific targets in the blood.

Since then, the use of tetramers has grown significantly. BRI serves as an international leader for the production and application of class II tetramers to improve the diagnosis and treatment of a wide variety of diseases. Tetramers are useful for a broad array of scientific advances. BRI scientists are using them to:

- Test the cellular response and efficacy of vaccines for several well-known and exotic viruses including influenza (seasonal and H1N1 “swine flu”), West Nile, Dengue fever, Japanese encephalitis (JEV) and yellow fever. West Nile, Dengue, JEV and yellow fever, also known as flaviviruses, are among the leading causes of sickness and death worldwide. BRI has a contract from the NIH to use tetramers to help assure that the most effective vaccines are being produced and developed.
- Identify and study immune responses to environmental allergens, including cat dander, tree and grass pollen, peanuts, mold and others. BRI has a contract from the National Institutes of Allergy and Infectious Diseases (NIAID) to research ways to use tetramers to monitor patients before and during desensitization to allergies.
- Isolate regulatory T cells that are important for fighting off the development of autoimmune disorders in Type 1 diabetes, multiple sclerosis, scleroderma and others. Design rapid blood tests to check whether new immunology treatments are working rather than waiting for long-term clinical results.

For more information on tetramers please visit BenaroyaResearch.org and search “tetramers.”

Jordan Brown Reports on Life with Diabetes

Jordan Brown, an 8-year-old BRI diabetes research participant, recently wrote a report for his health class on his experience with diabetes. Following is an excerpt.

“Many people are different in different ways. Some people have disabilities. Others have diseases or cancer. I have a special disease called Type 1 diabetes.

How it got to me, I’m not sure. But I can explain how it happens. Your white blood cells are sent to the pancreas by the immune system. When they reach the pancreas they attack beta cells, cells that produce insulin. Insulin is a liquid that breaks down blood glucose, sugar, in your blood to make energy.

What I have to do for this is multiple shots of insulin. When I eat food, I have to take a shot. This is because food contains carbohydrates. These increase blood sugar. Without insulin, I can get high blood sugar, which eventually leads to my death. It’s the same with too much insulin.

Another interesting fact is I am helping to prevent diabetes from happening to other people. You see, I have to fly to Seattle in a plane for a study. In this study, they attach a tube into my arm. The needle is about an inch long. The needle comes out, therefore leaving the tube. They draw blood from my arm and take A1C tests to see if I can take medicine (that is every once in a while). They put the medicine in the tube, it then goes through a filter and then through my veins. This helps the doctors understand how the medicine affects diabetes. My life is very different and cool.”



Jordan Brown participates in clinical research to help others with Type 1 diabetes.

For more information on diabetes clinical research, please visit www.benaroyaresearch.org/diabetes-research.

Grapes on the Green

Friday, Aug. 27, 6:30 p.m. — The Golf Club at Newcastle



To celebrate the end of the first day of Boeing Classic tournament play, The Golf Club at Newcastle will host the second annual Grapes on the Green event on Friday, Aug. 27. Proceeds from Grapes on the Green 2010 will raise support and awareness for two worthy local nonprofits: the Benaroya Research Institute at Virginia Mason and the Opportunity for Success Scholarship Fund.

The event will begin at 6:30 p.m. with a reception, which will feature wine tasting with select West Coast wineries. Guests will be joined at their table by local VIP guests for a multicourse dinner and an elite live auction featuring exclusive travel opportunities and rare wine lots.

The Grapes on the Green committee is comprised of these distinguished community leaders: Scott Oki, Chair, Geda and Phil Condit, Carolyn Corvi and John Bates, Molly Conner, Mary DeLancy, Larry Dickenson, Kathy Johanson, Sandy Gregory, Stacy Lill, Dana Lofton, Trish Markey and Julie Turnell.

The Boeing Classic is an official event on the PGA TOUR's Champions Tour. The 2010 Boeing Classic will feature golf legends like Mark O'Meara, Fred Funk, Nick Price, and Tom



Auctioneer John Curley with Phil Condit, Grapes on the Green committee member.

Kite and 2010 Champions Tour Rookies like Fred Couples and Corey Pavin. Over the past five years the Boeing Classic has raised nearly \$3 million for Virginia Mason Medical Center and additional Greater Seattle charities.

To learn more please call (206) 223-7504 or visit BoeingClassic.com.

Grant to Advance Cytoprotection for Tissue Injury

BRI received a \$2.8 million grant from the U.S. Department of Defense to advance work in cytoprotection for tissue injury through its Center for Control of Inflammation and Tissue Repair (CITR). The CITR research team, founded in 2007, has been working to develop new therapies to improve cell survival in the first hours after injury and generate new, engineered tissues to repair or replace tendons, ligaments, muscles and blood vessels. The new award focuses on "cytoprotection," using modulation of immune responses to control tissue damage from inflammation.

"We are actively seeking new solutions for patients who are faced with the prospect of losing life-sustaining tissue. This is an exciting project and we're pleased the Department of Defense chose to fund and support this important work," says Gerald Nepom, MD, PhD, Principal Investigator for the grant and Director of BRI.

BRI scientists will pursue a coordinated set of projects to develop and evaluate cytoprotective modulators of tissue-immune interactions which will improve cell survival. Another component of the new grant is to develop a "smart bandage,"



Robert Vernon, PhD, and Margaret Allen, MD, conduct research at BRI's Center for Control of Inflammation and Tissue Repair (CITR).

containing biological factors that would dampen local wound inflammation and promote healing. For more information on this grant, visit BenaroyaResearch.org and click on "news."

Dreambuilders' Ball Raises More Than \$1.1 Million

More than \$1.1 million was raised at the 19th annual Virginia Mason Dreambuilders' Ball to benefit autoimmune disease research at Benaroya Research Institute. More than 900 corporate and philanthropic community leaders attended the black-tie event, themed "Exploring the Mystery." BRI is grateful for the enormous community support at this event.

During the evening event, Sarah Penner shared her story of living with Type 1 diabetes and her participation in the clinical trial program at BRI. Carla Greenbaum, MD, described BRI's work in diabetes research. The event was co-chaired by Laura and Ian MacNeil and Kathleen Kobashi, MD, and Christopher Porter, MD. Presenting Sponsors KING-5 Television and The Benaroya Companies contributed significantly to the event's success.

The 2010 Dreambuilders' Ball honorees were Pamela and Joshua "Jay" Green, III, who have supported Virginia Mason Medical Center and BRI since the 1980s. Collectively, the two have given almost 25 years of leadership and service to the organizations. "I felt that our community needed this help, research and education for their families," says Pamela Green, who was a member of the BRI Board of Directors for eight years.



Jay and Pamela Green, III, were honored for their years of leadership and service.

Join Us for the Exciting Events at the Boeing Classic

The 2010 Boeing Classic, the annual PGA Tour Champions event benefiting the Benaroya Research Institute will be held Aug. 23 - 29 at TPC Snoqualmie Ridge golf course in Snoqualmie, Wash. Following is the schedule of events. For more information, visit BoeingClassic.com

Monday, Aug. 23 – Seahawks Rumble at the Ridge

Tuesday, Aug. 24 – Kids Clinic

Wednesday, Aug. 25 – Boeing Classic Pro-Am

Thursday, Aug. 26 – Boeing Classic Pro-Am

Friday, Aug. 27 – Boeing Classic Round 1

Saturday, Aug. 28 – Walk to Unlock the Immune System,
Boeing Classic Round 2

Sunday, Aug. 29 – Boeing Classic Round 3

Walk to Unlock the Immune System at the 2010 Boeing Classic

The 2010 Boeing Classic, the Annual PGA Tour Champions event, will include a 5k walk to raise funds and awareness for Benaroya Research Institute. The Walk to Unlock the Immune System will take place on Saturday, Aug. 28, prior to the second round of the Boeing Classic at TPC Snoqualmie Ridge Golf Course.

Registration for the walk will be \$25 and will include passes to the day's Boeing Classic tournament. The 54-hole event will take place at the TPC Snoqualmie Ridge, a private course designed by Jack Nicklaus. For tickets, volunteer opportunities or information on the Walk to Unlock the Immune System, please visit BoeingClassic.com.

Register for the Benaroya Research Institute Triathlon at Seafair

Athletes from all around the Pacific Northwest are swimming, cycling and running their way to fitness and athletic excellence in preparation for the Benaroya Research Institute Triathlon at Seafair on July 18. Seward Park on Lake Washington serves as a pristine venue for this sprint distance triathlon and offers an incredible experience for athletes of all ability levels. All donations from the event go to support autoimmune disease research of Type 1 diabetes, multiple sclerosis and rheumatoid arthritis at BRI. Please visit www.seafair.com/events/triathlon to register.



Swimmers race at the 2009 Benaroya Research Institute Triathlon at Seafair.

Jane Buckner, MD, Investigates How Autoimmune Diseases Work in Humans

Jane Buckner, MD, is a prominent scientist but she's also a physician — a specialist in rheumatoid diseases. She knows first-hand the pain and suffering of patients with diseases such as rheumatoid arthritis, lupus, relapsing polychondritis and other immune problems affecting the joints and connective tissues. Dr. Buckner's experience with patients inspires her to research for better treatments and cures for these devastating conditions.

Dr. Buckner wears three hats as a physician scientist. She leads her own research laboratory, directs the BRI Translational Research Program and sees patients as a rheumatologist at the Virginia Mason Medical Center.

The diseases she studies, Type 1 diabetes, rheumatoid arthritis, lupus, multiple sclerosis and relapsing polychondritis, can best be understood by studying the immune system. These diseases are caused when the immune system, designed to protect the body, attacks it instead. "My laboratory group works to understand why these diseases occur in people, how they happen and who they affect," says Dr. Buckner. "These diseases are very complicated. They behave differently in each patient, due to the influence of factors such as genetics and the environment. It's a challenge to understand the mechanism of these diseases within humans. However, success will directly translate into the development of new drugs and better therapies and the potential to individualize therapy for each patient."

Dr. Buckner's laboratory research explores these questions through a variety of BRI registries that contain human blood and tissue samples, medical histories and other data. Volunteer participants have donated these materials for study. The registries include information on people with autoimmune diseases and other immune-mediated diseases such as allergy and asthma. Diseases currently within the registries are multiple sclerosis, Type 1 diabetes, lupus, rheumatoid arthritis, scleroderma, inflammatory bowel disease, allergy, asthma, lung disease and transplant recipients. BRI also maintains a registry of healthy people for comparison purposes.

In her laboratory, Dr. Buckner looks at how regulatory T cells work. This group of white blood cells can block the activation of other harmful T cells and thus regulate the immune system, avoiding autoimmune diseases. Recently, Dr. Buckner and her team discovered that regulatory T cells are unable to suppress the cells that cause Type 1 diabetes, allowing these cells to cause disease. This knowledge will help in the development of

two modes of therapy that are both essential for eliminating Type 1 diabetes. One therapy will aim at increasing the number and strength of regulatory T cells in order to suppress the diabetes causing cells. The other therapy will attempt to make the diabetes causing cells more susceptible to suppression from regulatory T cells. This work can eventually be used across the spectrum of autoimmune diseases.



Jane Buckner, MD

As the Director of the Translational Research Program, Dr. Buckner is conducting studies with the registries to research the genetics that are linked to autoimmune diseases and to investigate what genes do to cause autoimmunity. This approach to understanding how genes contribute to autoimmunity has already been very productive. Dr. Buckner and her colleagues have shown how slight genetic variations can result in profound changes in T cells and B cells (both important in autoimmunity) in the people with these gene variants. Understanding these gene variants can help scientists determine how the immune response is altered in disease, why genes contribute to disease and help identify therapies that will intervene in this process.

"Translational research enhances our knowledge of why some people develop autoimmune disease by creating synergy between the basic science laboratory and clinical research studies," says Dr. Buckner. "With these three types of research — laboratory, translational and clinical — all being done in a collaborative atmosphere, we will be able to put all the pieces together to form a picture of disease that will help us to improve our patients' lives."

DID YOU KNOW?

Translational Research

Translational research takes laboratory discoveries from the bench to the bedside and back again. BRI has a strong commitment to translating new scientific knowledge into clinical trials for patients. Knowledge is translated not only from the laboratory to the bedside, but findings in clinical trials are brought back to the laboratory as well. For more information, visit BenaroyaResearch.org and click on "Translational Research Program."

Join Us at the BRI Open House at the Triathlon Expo

Benaroya Research Institute is hosting an open house at the 2010 BRI Triathlon Expo on July 17. Everyone is invited to tour a laboratory and view demonstrations of research being conducted at BRI. The Expo will have food and beverage samples from the Seafair sponsors, as well as giveaways and entertainment for the kids. It is the last chance to sign up for the Seafair Triathlon race and the only opportunity to pick up race materials. The Expo will be located in front of the BRI building on Ninth Avenue and Seneca Street in downtown Seattle. Whether you're joining the triathlon or not, you're welcome to attend the BRI Open House from 10:30 a.m. – 1 p.m. on Saturday, July 17.



Tour Benaroya Research Institute at the BRI Expo.

Learn About BRI Events and Sign Up for Our E-Updates and E-Newsletter

Visit our Web site for the latest information on clinical trials and research advances. Learn about our exciting events and sign up for our e-updates and e-newsletter at BenaroyaResearch.org.



Copyright ©2010 Benaroya Research Institute at Virginia Mason. All Rights Reserved.

Benaroya Research Institute at Virginia Mason (BRI) is an international leader in immune system and autoimmune disease research translating discoveries to real life applications. The BRI Newsletter is published several times throughout the year.

Benaroya Research Institute at Virginia Mason | 1201 Ninth Ave., Seattle, WA 98101 | BenaroyaResearch.org

RETURN SERVICE REQUESTED

1201 Ninth Ave.
Seattle, WA 98101-2795

UNLOCKING THE IMMUNE SYSTEM®
BENAROYA
RESEARCH INSTITUTE
VIRGINIA MASON