BRI Targets Type 1 Diabetes: From Discoveries to Innovative Therapies

Up to three million Americans have Type 1 diabetes, and the worldwide incidence of the disease is growing. In Type 1 diabetes, the body's immune system attacks and destroys the cells in the pancreas that make insulin. People with this disease must inject themselves with insulin to stay alive. They must carefully monitor their blood sugar levels and also balance their food intake and exercise.

For the past two decades, BRI has served as a worldwide leader in research to prevent, treat and cure Type 1 diabetes. BRI scientists have accounted for some of the substantial discoveries in the field, including the identification of diabetes susceptibility genes, descriptions of the properties of diabetes-associated immune cells, and the development of laboratory and clinical tools to study disease progression and response to therapy.

Current diabetes research at BRI ranges from making new discoveries in our laboratories to testing the most innovative therapies for patients. All five major divisions at BRI work on integrated and collaborative studies addressing important diabetes research questions. Our Translational Research Program at BRI studies how to design cells that regulate the immune system in individuals with Type 1 diabetes. Our Immunology Research Program looks for the critical molecular components that drive the autoimmune process that damages the pancreas. Our Hope Heart Matrix Biology Research Program is developing artificial tissues that will support islet cell replacement therapy and our Clinical Research Program supports clinical trial activities. In the Diabetes Research Program at BRI, dedicated physician-scientists build upon this broad know-how to conduct a wide range of clinical research immunotherapy trials for individuals diagnosed with Type 1 diabetes.

Clinical Research

- Carla Greenbaum, MD, heads the Diabetes Research Program at BRI, and is Principal Investigator for clinical trials with the goal of saving beta cells, which produce insulin. Her research focuses on the prevention and early treatment of Type 1 diabetes. She is joined by Principal

Investigators Srinath Sanda, MD, and Jenna Bollyky, MD, who conduct studies with research volunteers to find the best ways to measure the impact of changing immune activity on blood sugar control and islet survival. Asa K. Davis, PhD, recently joined the Diabetes Research Program as the Clinical Research Program Manager for the T1D Exchange Biobank, a program to connect diabetes patients with researchers around the world.

- BRI’s Diabetes Clinical Research Program also plays a leadership role in several national and international initiatives, acting as the Pacific Northwest Clinical Center for the National Institutes of Health TrialNet consortium, the JDRF Center for Translational Research and a clinical trial site for the Immune Tolerance Network.

- Patients and their families participate in BRI’s Diabetes Clinical Research Program through volunteering blood samples for research studies or by enrolling in clinical trials that test new ways to prevent Type 1 diabetes in people at risk or to preserve insulin secretion in people recently diagnosed. For people who have had (continued on page 5)
Recent Discovery Leads to New Approaches to Allergy Vaccine Therapy

A team of scientists at Benaroya Research Institute recently discovered how allergy shots steer the immune response to prevent allergies. These findings open new horizons for understanding allergic diseases and improving safety and efficacy of current allergy shots. The research results were recently published in the Journal of Allergy and Clinical Immunology.

“Allergy shots (allergy vaccine therapy) were introduced 100 years ago and remain the only curative treatment for certain types of allergies,” says Erik Wambre, PhD, BRI lead author of the study. “But scientists haven’t clearly understood how the immune system works to rid the body of the reaction to allergens.” Allergens are foreign substances that are usually considered harmless to the body, such as tree, grass and weed pollen, mold and dust mites, cat and dog dander, and food, such as milk and peanuts.

“Scientists thought that allergy shots strengthened the part of the immune system which controls the overacting allergic cells,” says Dr. Wambre. “But we found instead that the allergy shots cause repeated stimulation to the allergic immune cells and they become worn out and die.” This is a very important finding because scientists will use this information to develop better treatments for allergies including safer, more effective and faster therapies.

Researchers at BRI, including Dr. Wambre, William Kwok, PhD, and David Robinson, MD, Virginia Mason Allergy and Asthma Clinic, are taking a new approach to improve allergy vaccine therapy.

They are using tetramers — biomarkers discovered at BRI — to identify the piece of the allergen molecule (peptide) that causes a person to react. By using the peptide there potentially will be less side effects and the dose may be increased, hopefully leading to faster treatment. Patients can also be monitored closer with the use of tetramers.

Family Members Inspire Participation in Clinical Trials

Angelina Clarke spent years visiting multiple doctors and even had surgery, but they were unable to find the cause of her pain. In 2011, she came to Virginia Mason’s Digestive Disease Institute for a specialized procedure called a double balloon enteroscopy and met James Lord, MD, PhD, VM gastroenterologist and BRI Assistant Research Member. Based on her enteroscopy results, findings of her past doctors, and family history, Dr. Lord diagnosed her with Crohn’s disease. Crohn’s disease and ulcerative colitis (UC) are often referred to as inflammatory bowel disease (IBD).

In these diseases, the body’s immune system attacks the intestines, resulting in intestinal inflammation, abdominal pain and bleeding. IBD affects approximately 1.4 million Americans, evenly divided between UC and Crohn’s disease, and between men and women. It is more common in northern latitudes, like the Pacific Northwest, where an estimated 50,000 IBD patients reside.

Because her mom also has Crohn’s disease and she is worried about her son developing an autoimmune disease, Angelina felt that participating in the research at BRI was essential for her. “I think the research is important, if I can help even one person and make a difference, it will all be worth it.” She now is enrolled in the biorepository program at Benaroya Research Institute. The biorepository program allows scientists and doctors to study patients’ medical histories and data to understand disease treatment and progression.

Angelina is still getting used to the numerous diet and lifestyle changes, but feels her diagnosis and involvement in BRI research will continue to improve her life and the lives of those living with Crohn’s disease. For more information on inflammatory bowel disease, joining a registry and clinical trials, visit BenaroyaResearch.org.
Join Us in Eliminating Autoimmune Diseases
You Can Help as a BRI Champion

Our work would not be possible without the generous contributions from our friends and supporters. The BRI Champions Giving Circle is a newly formed giving circle, created to thank and recognize our donors’ commitment to BRI and to eliminating autoimmune diseases. Members will receive special updates from BRI Director, Gerald Nepom, MD, PhD, providing them with a first-hand look into the work happening in our laboratories to improve lives.

“I never understood how I ended up with all of these diseases, until I heard a talk from Dr. Nepom,” says Lauren Muffet, a supporter of BRI. “He explained that the underlying causes of my autoimmune diseases may be interconnected. It makes me feel relieved and hopeful to know that there are highly skilled people dedicated to improving my quality of life through research. Relieved to know that I am not alone and hopeful that one day there will be a cure. This is why I am a strong advocate and supporter of BRI. The Institute's research has a direct impact on my life and the lives of others who must deal with autoimmune diseases every day.”

BRI Champions puts the resources needed in the hands of the scientists conducting cutting-edge research. Progress is being made, and while we are still working to find a cure, we are able to provide better treatment options to the millions of people living with autoimmune diseases.

We invite you to join the BRI Champions Giving Circle. Your annual contribution of $1,000 or more will help us to continue our life-changing research and bring hope for the future. For more information about becoming a BRI Champion, please contact D’Nika Jackson at (206) 341-1337 or dnika.jackson@vmmc.org.

The Seattle Foundation Provides Grant for Cell Analysis Instrumentation

The latest technology allows scientists to analyze cells at the rate of 25,000 per second. For autoimmune disease research, it is vital to use state-of-the-art instrumentation to select, sort and identify the cells that cause autoimmune diseases. Then scientists can study how autoimmunity works and find ways to prevent and treat disease. BRI is very dependent on its five cell analyzing flow cytometers and two high-speed cell sorters in the Flow Cytometry Core Laboratory. These instruments are being used around-the-clock and are booked weeks in advance.

A recent grant of $50,000 from The Seattle Foundation will support the purchase of an additional analyzing flow cytometer, providing a critical resource for more than ten principal investigators and multiple research projects. “Different protein molecules can be tagged with different antibodies that are stained with a unique color of fluorochrome. Lasers are used to separate these by color, size or shape,” says K. Arumuganathan, PhD, Manager of the Flow Cytometry Core. “Then the data is instantly graphed and the scientists can analyze it. This new instrumentation will help immensely to speed up the rate of research. We also have cells that need to be analyzed quickly and this will help with our efforts to meet scientists’ needs. We are grateful to The Seattle Foundation for their support.”
Register Now for the 2012 BRI Seafair Triathlon

The Benaroya Research Institute Seafair Triathlon and Kids Triathlon will take place on Sunday, July 22. Thousands of athletes from around the Pacific Northwest will gather at Seward Park in Seattle to swim, cycle and run in what was voted the best sprint and Olympic triathlons in the region. Both courses take athletes of all ability levels on a flat, scenic journey around Lake Washington — come test your skills and set a new personal record!

Kids can participate too. Following the adult triathlon, kids will have a chance to challenge themselves with one of two categories of races based on skill level. For more information or to register, please visit Seafair.org.

Hear from Experts at the Diabetes Expo

The American Diabetes Association Expo is a free event held at the Washington State Convention Center on Saturday, April 21, and includes health screenings, cooking demonstrations, and product and service exhibitors. Leading experts from BRI and other community diabetes organizations will be talking about diabetes management and prevention. For more information call 1-888-DIABETES (342-2383).

Schedule a Talk at Your Next Meeting

The Benaroya Research Institute Speakers Bureau provides background on autoimmune diseases and information on the research being conducted at BRI to find the causes and cures for these diseases. The speakers bureau program includes lay and scientist speakers, powerful personal stories about autoimmune diseases and time for audience questions. Our specially-trained speakers are BRI board members, scientists and volunteers who have been affected by autoimmune diseases and are committed to sharing the groundbreaking research happening in our community.

To schedule a presentation or for more information, please contact Rachel Martin at rmartin@benaroyaresearch.org or (206) 342-6519.

Walk to Raise Funds for Multiple Sclerosis Research

The South Sound and Seattle Walk MS events are the rallying points of the MS Movement, a community coming together to raise funds for the Greater Northwest Chapter of the Multiple Sclerosis Society and celebrate hope for the future. The Greater Northwest Chapter of the MS Society is excited to offer new locations and features for the 2012 Walk MS events.

The South Sound Walk will be held on Saturday, April 14, at the new location of Chambers Creek Properties, next to Chambers Bay Golf Course in Tacoma. The Seattle Walk on Sunday, April 15, is moving out of the chilly spring weather into the Alaska Airlines Arena at the University of Washington. For more information about the Walk MS events or to register, please visit walkMSnorthwest.org.

See the Latest Research at BRI’s Science Friday

Science Friday is an opportunity to learn about the remarkable discoveries taking place at Benaroya Research Institute. The free event includes a light breakfast and conversation with Gerald Nepom, MD, PhD, Director of BRI, and a laboratory tour and discussion led by BRI scientists.

Sign up for 2012 Science Friday dates: April 20, July 20 and Oct. 19 by contacting Rachel Martin at (206) 342-6519 or rmartin@benaroyaresearch.org.

Robert Vernon, PhD, is one of the scientists leading tours at BRI.
Autoimmune diseases are caused in part by the inheritance of genes that increase a person’s susceptibility. Studying these gene variants is critical to understanding autoimmune diseases. Benaroya Research Institute has created a Genotyping Core Laboratory to help identify and analyze gene variants. Karen Cerosaletti, PhD, manages the laboratory as well as pursing her own genetics research and collaborating on other genetic projects.

Using the latest technology, the laboratory can analyze the DNA of people with autoimmune diseases for gene variants that have been identified as important in a wide variety of autoimmune diseases including Type 1 diabetes, multiple sclerosis, lupus, rheumatoid arthritis, inflammatory bowel disease and others. The core laboratory has genotyped a large percentage of participants in the BRI disease registries to help scientists study these disease variants. A registry of healthy people also helps to compare the genetic variants in health and disease.

Dr. Cerosaletti and collaborators are finding that genetic variants can affect cells in a variety of ways across a number of autoimmune diseases. Gene variants can affect the growth of regulatory T cells that keep the immune system in balance. They can also affect the signals from growth factors that can drive immune cells to become inflammatory (destructive) or protective.

“With the new addition of Systems Immunology to BRI, we hope to synthesize all of the genetic and immunologic data collected on an individual so we can study in-depth the person’s disease, disease progression, effects of therapies and outcomes. This will give us a much deeper understanding of autoimmune diseases and how to develop new treatments.”

Scientist Uses Genetics to Help Solve Autoimmune Diseases

BRI THROUGH THE MICROSCOPE

BRI Targets Type 1 Diabetes (continued from front cover)

diabetes for a long time, our research aims to find ways that allow replacement islets to avoid immune attack, an important element in developing a successful therapy.

Laboratory Research

- Jane Buckner, MD, BRI Associate Director, is studying how immune regulation is lost in Type 1 diabetes. Her lab has discovered that the T cells of people with diabetes fail to respond to several molecules that are a vital part of the body’s system of protection from autoimmunity.

- Gerald Nepom, MD, PhD, BRI Director, studies how genetic elements control signals that direct immune responses to attack pancreatic islet cells, helping to understand why different people develop disease and respond to therapy in different ways.

- BRI’s bioengineered islet implant project aims to develop an implantable device comprised of natural, collagen-based biomaterials that supports transplantation and survival of insulin-producing cells.

- Karen Cerosaletti, PhD, directs a research effort to explain molecular mechanisms that confer susceptibility to Type 1 diabetes.

- William Kwok, PhD, leads a team that produces biomarkers, called tetramers, which measure the destructive immune responses that underlie Type 1 diabetes.

- Helena Reijonen, PhD, works on finding ways to use these tetramers for better prediction of a person’s disease risk and in monitoring the outcome of immunotherapy in clinical trials of Type 1 diabetes drug therapies.

- Damien Chaussabel, PhD, leads a team of scientists and bioinformatics specialists who analyze changes in expression of genes. Patterns unmasked by this work illustrate fundamental properties of the disease process, looking comprehensively at the way diabetes changes over time, and after therapy.

- Steven Ziegler, PhD, and Daniel Campbell, PhD, direct laboratory studies using preclinical model systems to help evaluate efficacy of experimental therapies targeted against diabetes before these therapies are used in clinical trials.

For more information call (800) 888-4187 or visit BenaroyaResearch.org/diabetes-research.
Autoimmune Advocacy Alliance Presents
Seattle Autoimmunity Day

Seattle Autoimmunity Day will be held May 19 at the Volney Richmond Auditorium at Virginia Mason Medical Center. The educational forum will feature prominent keynote speakers who work in the field of autoimmune diseases as well as a patient panel of people living with such conditions as Type 1 diabetes, multiple sclerosis, rheumatoid arthritis, Crohn’s disease, lupus, celiac disease or others of the more than 80 autoimmune diseases. Autoimmune Advocacy Alliance (A3) brings together advocacy groups, health professionals and individuals interested in furthering the understanding and treatments for autoimmune disease. For more information, please visit a3autoimmunity.org.

Sign Up for Our E-Updates and E-Newsletter

Visit our website for the latest information on research, clinical trials and bioregistries and to sign up for our e-updates at BenaroyaResearch.org.