



## BRI Expands Multiple Sclerosis Research

**M**ultiple sclerosis (MS) is a chronic, often disabling, autoimmune disease that attacks the central nervous system, affecting an estimated 400,000 people in the United States. MS is more prevalent in the Northwest region than almost anywhere else in the world.

BRI has a strong basic, translational and clinical MS research program including extensive experience in clinical trials with the most recent and dramatically efficacious immunotherapies. Recently, A. Scott Nielsen, MD, a neurologist and MS researcher from Harvard Medical School, joined Benaroya Research Institute at Virginia Mason (BRI) as a Principal Investigator. He will also serve as a clinician at the Virginia Mason Multiple Sclerosis Center. Dr. Nielsen brings additional expertise to the MS team and will launch new research studies. (See more on Dr. Nielsen in "Researcher in the Spotlight," on page 5.)

MS occurs when the body's immune system mistakenly attacks myelin, the fatty substance that surrounds and protects the nerve fibers in the central nervous system. When the myelin is damaged the nerve impulses are not transmitted as quickly or efficiently, resulting in symptoms such as numbness in the limbs, fatigue, dizziness, paralysis and/or loss of vision. Symptoms of MS will often improve and relapse with time and vary from one person to another. In progressive forms of multiple sclerosis, they gradually worsen.

Following is an update on BRI's MS research:

### Clinical Research

- Five clinical research trials in MS are currently being conducted at BRI. The newest study is an Immune Tolerance Network (ITN) study that is evaluating the efficacy and safety of Abatacept in adult patients with relapsing-remitting multiple sclerosis (RRMS). RRMS is the most common form of MS. Abatacept is a biologic drug that selectively modulates the body's immune system. It has been approved by the FDA for the treatment of moderate-to-severe rheumatoid arthritis in adults.



Estelle Bettelli, PhD, and Mariko Kita, MD, are part of the BRI team looking for better treatments for multiple sclerosis.

- Other active trials include testing several oral medications to find out if they can decrease the number of MS relapses during a certain time period for RRMS, comparing the use of a combination of drugs versus using the drugs alone in RRMS and testing different doses of different drugs in RRMS.

### Laboratory Research

- Estelle Bettelli, PhD, BRI Principal Investigator, along with other scientists, discovered a subset of immune system cells which are believed to be potent inducers of MS and other autoimmune diseases. She is studying these cells to determine how to inhibit their harmful function. She also developed system models which can replicate different forms of MS to understand how the different arms of the immune system influence disease development and progression.

### Translational Research

- Karen Cerosaletti, PhD, BRI faculty member in the Translational Research Program, is studying MS to better understand the nature of disease initiation and progression. Her work focuses on developing novel

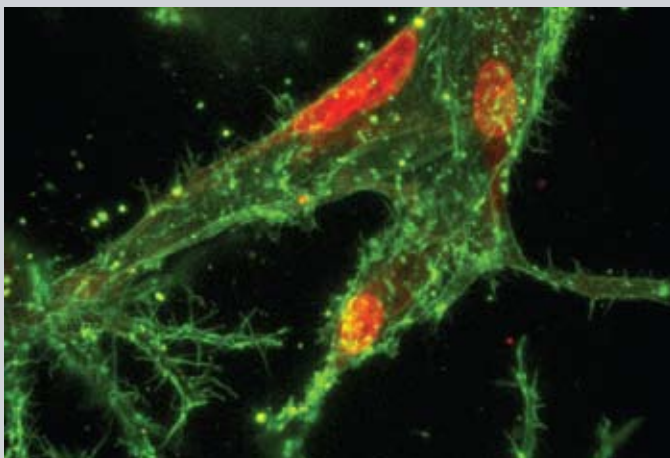
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## New Microscope Shows Cells in 3D

The cells of the body are organized in three dimensions (3D), but biomedical research is often conducted in two dimensions – on thin slices of tissue or on cells grown in flat-bottomed dishes. Imagine, instead, that you could look into an artificial blood vessel to evaluate its design in 3D or watch immune cells interact in 3D environments that simulate the body's own tissue. Benaroya Research Institute now has this capacity through purchase of a state-of-the-art confocal microscope, funded by the U.S. Department of Defense.

“With confocal microscopy, we can analyze the 3D structure of body tissues or the organization of cells grown in 3D collagen gels that simulate native connective tissues. Moreover, we can follow the behaviors of living cells using time-lapse photography,” says Robert Vernon, PhD, Director of BRI’s Histology/Imaging Core. The heart of the confocal system consists of four lasers that scan through the tissue to light up fluorescent dyes. The dyes emit different colors that can reveal cells, cell structures, or even the location of specific types of molecules. A high-resolution 3D image can be produced by scanning the tissue at different depths and combining the scans digitally.

The confocal microscope will be used for projects throughout BRI that include bioengineering replacements for diseased or injured tissues, studies of blood vessel growth in health and disease and investigations of the interactions between immune cells and connective tissues that may influence how immune cells fight disease.



Cells taken from the lining of human blood vessels and cultured for four days in a 3-dimensional collagen gel have organized into hollow tubes that resemble capillaries – the smallest form of blood vessel. Image courtesy of Michel Gooden (Vernon Lab).

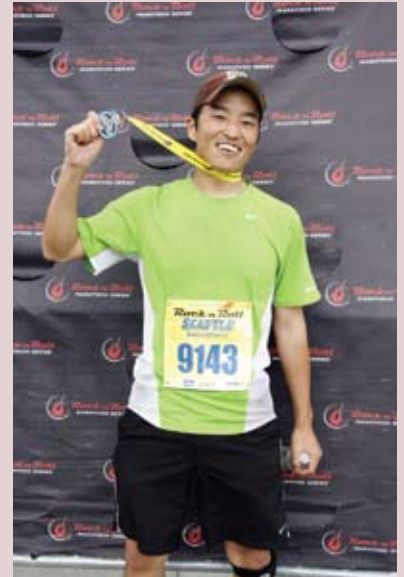
## Marathoner Uses Diabetes as an Educational Opportunity

In 2010, Michael Kim was so busy concentrating on his first year of law school at the University of Washington and training for his first marathon, he did not notice his extreme thirst and constant need to use the bathroom.

At a checkup, Michael’s blood glucose levels were extremely high and he was diagnosed with Type 1 diabetes also called juvenile diabetes or autoimmune diabetes. Diabetes is a chronic, debilitating disease which affects more than 20 million Americans. In diabetes, the body does not produce or properly use insulin. There are generally two types of diabetes—Type 1 and Type 2. In Type 1 diabetes, the body’s immune system attacks and destroys the cells that make insulin.

Michael did not know anyone else with Type 1 diabetes so he turned to the University of Washington Diabetes Care Center for help and education. The staff helped Michael learn to modify his diet, insulin injections and exercise to control his blood glucose level. They also told him about the groundbreaking diabetes research being done at Benaroya Research Institute and that he could be a part of it. Michael provides blood samples to BRI scientists striving to find new ways to eliminate the disease.

Michael competed in the June Rock n’ Roll Marathon in Seattle and is becoming more conscious of his diet. He is using his diagnosis to raise awareness among his friends, family and classmates about Type 1 diabetes and to teach them about the research conducted at BRI and in the community to eliminate autoimmune diseases. For more information about joining a registry or clinical study, visit [BenaroyaResearch.org](http://BenaroyaResearch.org).



Michael Kim, diabetes research participant, completes the Rock n’ Roll Marathon in Seattle.

## A Family Foundation Helps Fund Research at BRI

The Klorfine family was introduced to Benaroya Research Institute in 2005. Leonard Klorfine was impressed by BRI's approach to research of the immune system, auto-immune diseases and tissue engineering. They became further engaged in supporting BRI in 2009 after attending the Dreambuilders' Ball event. Shortly after, Leonard and his son, Stuart, met BRI Director Gerald Nepom, MD, PhD, and Robert Vernon, PhD, Research Associate Member, while touring the labs at BRI. "We were amazed by the groundbreaking research at BRI and wanted to support their incredible work," said Leonard Klorfine.

The Klorfine Foundation has been a supporter of the Vernon Laboratory within the Hope Heart Matrix Biology Program at BRI. The support has been important to Dr. Vernon's work to develop new, engineered tissues to repair or replace tendons, ligaments, skin and blood vessels, and also a pancreatic islet implant to treat Type 1 diabetes.

"The continued support of the Klorfine Foundation has been very important to our work. Their funding has helped these projects progress through the early phases to yield mature prototypes that are ready for more rigorous testing," says Dr. Vernon. "The Klorfine Foundation's contributions have also helped us to collect data instrumental for the development of proposals for federal funding to



Stuart and Leonard Klorfine discuss the latest developments in research with Robert Vernon, PhD.

sustain our work and increase our productivity."

The Klorfine Foundation was founded by Norma and Leonard Klorfine. Based in Philadelphia, the foundation has provided strong support to the arts since its formation, and is increasingly supporting environmental and scientific organizations, such as BRI.

For more information on giving to Benaroya Research Institute, visit [BenaroyaResearch.org](http://BenaroyaResearch.org) and click on Donate Now. To talk to someone about a gift, please call Jeanne Jachim at (206) 583-6083.

## BRI Tracks Emerging Infectious Diseases with New Methods

New efforts to improve global health will be launched by Benaroya Research Institute with a \$5.3 million grant from the National Institutes of Health (NIH) through the National Institute of Allergy and Infectious Diseases (NIAID). Using novel blood profiling technologies, BRI will study emerging and re-emerging infectious diseases that affect millions worldwide.

"We can study the blood of the people who have symptoms of infectious diseases and use biomarkers to accomplish several things," said Damien Chaussabel, PhD, Director, Systems Immunology Division at BRI. "We can use the markers to determine the type of disease which is sometimes hard to diagnose. We can also determine the severity of the disease and whether treatments are working. This will help to triage the patients needing more or different treatment or even hospitalization. We can also learn about emerging epidemics and how diseases can spread.

"We use new cutting-edge technologies that provide great benefits. First, they are fast — the test results can be obtained in a few hours rather than the usual 24 to 48 hours. Second, they are sensitive — they can identify

the disease even when it is no longer present in the bloodstream. Third, they can predict disease severity and predict outcome. Fourth, they are cost effective. Another benefit is the test is easy to do in the field with just a couple drops of blood," explains Dr. Chaussabel.

BRI and collaborators will be studying three different infectious diseases that constitute significant public health burdens in three distinct geographical areas: Sepsis Diseases in Thailand, Diarrheal Diseases in Mexico and Brucellosis in Macedonia.

"This grant allows us to pursue an alternative diagnostic system that we hope will save many lives," says Dr. Chaussabel.



Dr. Chaussabel uses blood profiling technologies to diagnose and follow infectious diseases.

## Autoimmune Disease Research Benefits From Boeing Classic

The 2011 Boeing Classic Golf Tournament on Aug. 22 - 28 was hailed a success with more than 60,000 visitors, raising funds for Benaroya Research Institute.



Gerald Nepom, MD, PhD, BRI Director, and Trish Markey, Grapes on the Green Committee Member and BRI Board Member.

To celebrate the first day of tournament play Aug. 26, The Golf Club at Newcastle hosted the second annual Grapes on the Green event. Donations from the event will help support

BRI's research to eliminate autoimmune diseases.

"We want to thank all the spectators, volunteers, golfers and partners that helped make the 2011 Boeing Classic so successful," says Jack Nagan, Executive Director of BRI. "This event has increased public awareness of the devastating impact of autoimmune diseases and raised support to accelerate research of these diseases."

## BRI Represents Life Sciences for Seattle Study Mission

Benaroya Research Institute was selected to represent the Life Sciences Industry at the Seattle Study Mission, a senior-level delegation of regional business, government and civic leaders. The mission was created by the Seattle Chamber of Commerce and the City of Seattle to showcase innovative regional organizations. Members received a high-level tour of the groundbreaking research occurring at BRI on June 30.



BRI representatives standing, L - R, Thomas Wight, PhD, Director of Hope Heart Matrix Biology Program, Jack Nagan, Executive Director, Jerry Nepom, MD, PhD, Director

## The Sun Shines on the BRI Triathlon at Seafair

Triathletes and spectators appreciated the sun shining at the Benaroya Research Institute Expo and Triathlon at Seafair on July 23 and 24. More than \$18,000 was raised to sup-



Seafair representatives have fun with Tommy T Cell, BRI's mascot.

port BRI's research for Type 1 diabetes, multiple sclerosis and rheumatoid arthritis.

The Triathlon Expo offered participants the opportunity to tour BRI and witness the Institute's cutting-edge research. Three scientists discussed studies in Type 1 diabetes, tissue engineering and molecular profiling.

The 11th annual BRI Seafair Triathlon was the first year for an Olympic distance triathlon event. Nearly 2,000 Olympic, sprint and kids triathletes swam, biked and ran through the beautiful setting of Seward Park in Seattle. Thank you to the many athletes, sponsors and volunteers that made this event so successful.

## New Web Site Makes Screening for Type 1 Diabetes Easy

People with a family member with Type 1 diabetes are 15 times more likely to develop the disease. If someone in your family has Type 1 diabetes, the rest of the family can be screened



for free. A new interactive Web site for Type 1 diabetes screening called "Pathway to Prevention" provides locations for screening and other important information.

A simple blood test could detect an increased risk for Type 1 diabetes years before symptoms appear. If family members are at increased risk, they may be eligible to participate in clinical trials that are testing ways to prevent and delay Type 1 diabetes. This test is available to eligible family members of people with Type 1 diabetes through an international research effort led by the National Institutes of Health. Visit [TrialNetPathwayToPrevention.org](http://TrialNetPathwayToPrevention.org) to learn more about screening.

## New Researcher to Explore Options for Patients With MS



A. Scott Nielsen, MD, recently joined BRI and will increase MS clinical research opportunities.

**B**enaroya Research Institute welcomes A. Scott Nielsen, MD, as a BRI Principal Investigator for MS studies and a clinician at the Multiple Sclerosis Center at Virginia Mason. Dr. Nielsen will work with the director of the center, Mariko Kita, MD, BRI Principal Investigator, to expand patient options for research study participation.

Dr. Nielsen's interests include:

- Exploring new cutting-edge research options to improve treatments for MS.
- Studying the use of medications for MS that increase mobility in combination with rehabilitation exercises to improve patients' functionality.
- Using a rich database of patient information to understand the impact of MS on patients' cognitive ability, better define MS biomarkers and use biomarkers for future interventional studies including experimental therapeutics.
- Improving the delivery of care by researching the health of patients with MS over time.

Dr. Nielsen previously served as a researcher and clinician at Harvard Medical School, Beth Israel Deaconess Medical Center and Massachusetts General Hospital, in Boston.

## Sign Up for Our E-Updates and E-Newsletter

Visit our Web site for the latest information on research and sign up for our e-updates at [BenaroyaResearch.org](http://BenaroyaResearch.org).

## BRI Expands MS Research

*(continued from front cover)*

biometric tools, called "tetramers," for monitoring disease prognosis and progression, and for evaluating the response to therapy in MS. These tetramers were developed and produced in BRI's tetramer production facility.

- Another area of MS research at BRI focuses on discovering why some RRMS patients are more resistant to treatment than others. The goal of these studies, led by Jane Buckner, MD, BRI Translational Research Program Director, is to determine why the myelin specific T cells in MS patients are not "turned off" by the immune systems regulatory responses. This breakdown in the systems that control autoimmunity may be the key to why MS patients have flares of their disease and could be a target of therapy. BRI's current studies now focus on understanding how we can reverse the process of failed regulation during an MS flare.

### Systems Immunology

- In 2011, Damien Chaussabel, PhD, joined BRI to launch the Systems Immunology Division that will develop a way to profile people's immune systems to pioneer new approaches to diagnosis, prognosis and therapy.

For more information on MS clinical trials and the registry, visit [BenaroyaResearch.org](http://BenaroyaResearch.org).

## Multiple Sclerosis Prevalence in the Northwest

MS affects approximately 400,000 Americans (1 in 1,000), but is much more common in the Northwest where approximately 12,000 (2 in 1,000) people have MS. Some likely factors that contribute to this geographic effect are vitamin D deficiency from lack of natural sunlight, genetic predisposition in the North European/Scandinavian heritage and an environmental trigger, possibly a virus, found between 20 and 40 degrees latitude worldwide. Other factors are still unknown.

# Save the Date for Upcoming Events

## October 8 – Step Out: Walk to Stop Diabetes

The America Diabetes Association annual fundraising walk will take place at Magnuson Park in Seattle at 9:00 a.m. For more information, please visit [stepout.diabetes.org](http://stepout.diabetes.org).

## October 21 – Science Friday

A breakfast event that includes a conversation with Jerry Nepom, MD, PhD, Director of BRI and a laboratory tour of BRI led by scientists. To sign up or for more information, please visit [BenaroyaResearch.org](http://BenaroyaResearch.org).

## November 4 – Illuminations Luncheon Fundraising Event for Benaroya Research Institute

A luncheon and program at the Heritage Room, the Rainier Club. For more details, please visit [BenaroyaResearch.org](http://BenaroyaResearch.org).

## November 4 - 6 – Life Sciences Research Weekend at Pacific Science Center

BRI will team up with the Northwest Association for Biomedical Research, Pacific Science Center and other area organizations for three days of demonstrations, interactive exhibits and talks. For more information, please visit, [nwabr.org/community/life-sciences-research-weekend](http://nwabr.org/community/life-sciences-research-weekend).

## Speakers Bureau

Book the BRI Speaker Bureau for your next meeting or event. For more information, please visit [BenaroyaResearch.org](http://BenaroyaResearch.org).



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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.



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