



BRI Makes Advances in Inflammatory Bowel Disease Research

Inflammatory bowel disease (IBD) refers to two different diseases – Crohn’s disease and ulcerative colitis (UC). In these diseases, the body’s immune system mistakenly attacks the intestines, resulting in intestinal inflammation, abdominal pain and bleeding. IBD usually strikes people early in life, leading to many years of suffering and disability. IBD affects approximately 1.4 million Americans (almost 1 in 200), 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. 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 unknown environmental triggers.

Crohn’s disease and UC differ primarily in where the inflammation occurs. In UC, inflammation is contiguous and limited to the lining (or “mucosa”) of the colon. Crohn’s disease can be patchy, and can involve any location in the gastrointestinal tract, but most commonly involves the last part of the small intestine (called the ileum) and the colon. Inflammation in Crohn’s can burrow beneath the mucosa, causing scarring, abscesses, or leaking holes called fistulas. At Benaroya Research Institute at Virginia Mason (BRI) immunology research in these diseases focuses on understanding the processes that initiate and perpetuate the inflammation, on designing targeted immune therapies to block or reverse these processes, and on clinical trials to evaluate effectiveness and safety of immune modulation in patients with ongoing disease.

BRI works closely with the Digestive Disease Institute (DDI) at Virginia Mason Medical Center (VMMC), where approximately 2,000 IBD patients are followed by one of the most highly acclaimed gastroenterology divisions in the U.S. The DDI maintains a robust IBD clinical research program with extensive experience in national clinical trials including past studies with abatacept and natalizumab, and ongoing studies with even more novel immunotherapies.

Clinical Research

- Clinical trials are led by James Lord, MD, PhD, BRI Principal Investigator, and Richard Kozarek, MD, the Executive Director of the DDI and current President of the World Gastroenterology Organization.



Research participant, Susan Richardson, discusses upcoming clinical research trials with James Lord, MD.

- Two clinical research trials in IBD are currently being conducted at VMMC/BRI. The newest study is an industry-sponsored clinical trial evaluating the efficacy and safety of an oral medication that is an inhibitor of a certain molecule on immune system cells. The trial, currently open for enrollment, is for adults with Crohn’s disease.
- An IBD database is tracking clinical outcomes and important metrics of quality care in all patients with IBD at VMMC.

Laboratory Research

- Dr. Lord has established an IBD-specific clinic at VMMC, and is supported at BRI by a grant from the National Institutes of Health (NIH) to research the interactions between the intestinal mucosa and the regulatory mechanisms of the immune system, to better understand how these mechanisms break down in IBD. He established the IBD biorepositories

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Researchers to Study Role of Iron in Liver Disease

Benaroya Research Institute received a new \$2.5 million grant from the National Institutes of Health (NIH) to study the role of iron in the most common liver disease in the U.S., non-alcoholic fatty liver disease (NAFLD). Principal Investigator for the grant is BRI Clinical Researcher Kris Kowdley, MD. Dr. Kowdley is also Director of Research and Director of the Liver Center of Excellence at the Digestive Disease Institute at Virginia Mason Medical Center.

Up to 30 percent of people in the U.S. may be affected by NAFLD, and 3 to 4 percent may have a serious form of this disease called non-alcoholic steatohepatitis (NASH). Also, more than two million Americans are at risk of developing cirrhosis of the liver from this disease. NAFLD is a serious condition that occurs when too much fat builds up within the liver, in the absence of excessive alcohol use. This liver disease is associated with obesity, diabetes, elevated lipid levels, hypertension and cardiovascular disease. In some individuals, the accumulation of fat causes inflammation called steatohepatitis (NASH) that damages the liver. NASH is one of the leading causes of cirrhosis of the liver in the U.S. Liver disease also increases the risk of diabetes, cancer and heart disease.



Kris Kowdley, MD, is Principal Investigator for the new liver disease grant.

Cirrhosis is a condition in which the liver becomes progressively scarred. With progressive cirrhosis, the liver is unable to function properly and a liver transplant may be needed.

“Our previous research suggests that one-third of Americans with NAFLD have iron deposits in the liver which may contribute to disease progression,” said Dr. Kowdley. “There is an urgent need to understand the mechanisms leading to NASH, including the role of iron. Our goal is to understand the causes of this common but poorly understood liver disease in the hopes of developing new therapeutic interventions.”

For more information visit BenaroyaResearch.org.

Arthritis Research Participant Finds Value in Study

For nearly five years, Elizabeth Moseley suffered silently. Soreness in her back at age 19 grew to an excruciating pain throughout her entire body. Both Elizabeth’s maternal grandmother and great-grandmother were diagnosed with rheumatoid arthritis (RA), an autoimmune disease that causes painful swelling of the joints and surrounding tissues, as very young women. Scared of the possible diagnosis, Elizabeth kept her agony silent until the pain grew to be unbearable and a Port Townsend urgent care clinic physician diagnosed her with a different autoimmune disease, lupus.



Elizabeth Moseley (center) with her parents.

Elizabeth nervously read up on this puzzling disease awaiting her referral to Jeffrey Carlin, MD, head of rheumatology at Virginia Mason Medical Center. On Nov. 14, 2010, Dr. Carlin changed her diagnosis to rheumatoid arthritis. Lupus and RA can be difficult to differentiate at the onset, but the diagnosis of a more familiar disease was suddenly welcome news.

After months of standard treatments, Elizabeth’s pain had lessened but her joints remained swollen and tender. Dr. Carlin suggested that she consider joining a clinical trial being conducted by Stanford Peng, MD, PhD, Clinician Researcher at Benaroya Research Institute. The study involves a musculoskeletal ultrasound, a way to assess arthritis which may be more objective than physical examination, and a mixture of medications to lower disease activity or send it into remission. She admits to initially being nervous about the trial but since her progress stalled, she enrolled.

Elizabeth is participating in a six-month trial and her symptoms are going into remission. With no regret for her decision, her life is literally back in motion. You might catch her commuting daily by bike from Magnolia to Eastlake to her new baking job – if you can keep up.

For more information on rheumatoid arthritis, joining a registry and clinical trials, visit BenaroyaResearch.org.

Friends Honor Dave Fanning by Giving to BRI

The David J. Fanning Memorial Golf Tournament was started by a group of friends in June 2011 to honor David Fanning. Dave, who passed away on June 14, 2010, was a devoted husband and father, respected businessman and an avid golfer.

The tournament is an opportunity for friends and family to share memories about Dave while playing a game he enjoyed and supporting a cause he was passionate about – finding a cure for Type 1 diabetes. Benaroya Research Institute was chosen to be the beneficiary of the event because of its mission to eliminate autoimmune diseases and its innovative Type 1 diabetes research program.

More than 80 players enjoyed a round of golf at the beautiful Tumble Creek Club at Suncadia Resort on June 28, 2011. With the help of corporate sponsorships and individual donations, more than \$19,000 was raised for Type 1 diabetes research at BRI. The organizers were pleased with the results and are looking ahead to the 2012 David J. Fanning Memorial Golf Tournament.

“We are so grateful to the players and corporate sponsors who took it upon themselves to support the first David J. Fanning Memorial Golf Tournament,” says Steve Gillis,



Friends remember Dave Fanning with a golf tournament that benefits BRI.

longtime friend and colleague of Dave Fanning. “The great turnout and the ability to support the Benaroya Research Institute is a true testament to Dave’s memory. We look forward to teeing it up again next year.”

For more information on giving to Benaroya Research Institute, visit BenaroyaResearch.org and click on Donate Now.

BRI Investigates Ways to Create Blood Vessel Replacements

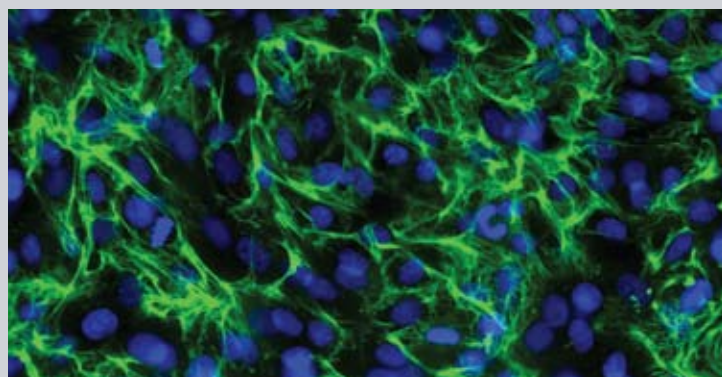
Benaroya Research Institute received a new \$2.4 million grant from the National Institutes of Health to develop tissue-engineered replacements for blood vessels that have been damaged or lost through disease or injury. Principal Investigators for the grant are Robert B. Vernon, PhD, and Thomas N. Wight, PhD, of the Hope Heart Matrix Biology Program at BRI.

More than four million people in the U.S. are affected by arterial disease, with approximately 600,000 having bypass procedures each year to restore blood flow to their major organs or limbs. In general, the patient’s own blood vessels are the “gold standard” for replacement of diseased arteries. However, a substantial number of patients lack suitable blood vessels for grafting, and there is a need for alternatives. There is also a need to provide vascular shunts for dialysis patients and replacements for blood vessels damaged or lost by trauma. Replacements for blood vessels have been made from synthetic materials, but they have not yet proven to be completely satisfactory.

As an alternative to synthetic blood vessels, BRI is developing biologically based blood vessel replacements

made from living cells seeded into prefabricated supports (scaffolds). To promote healing of the vascular graft, the scaffolds are made from structural molecules found in natural connective tissues. These tissue-engineered blood vessels, which ultimately would incorporate the patient’s own cells to limit rejection, may be the best approach to generate vascular grafts that function in all respects like natural blood vessels.

For more information, please visit BenaroyaResearch.org.



Cells isolated from the wall of a blood vessel are stimulated to produce fibers of elastin (green).

Illuminations Raises Support for the Future of Immunology



Illuminations Luncheon Emcee Steve Raible, KIRO 7 News Anchor; Kristi Pangrazio, Event Chair; Gerald Nepom, MD, PhD, Director of BRI; and Damien Chaussabel, Keynote Speaker.

Illuminations, the inaugural fundraising luncheon benefiting Benaroya Research Institute, was a great success. Guests filled the ballroom at the Rainier Club in Seattle to hear Gerald Nepom, MD, PhD, Director of BRI, describe the work being done at BRI to eliminate autoimmune diseases.

BRI Systems Immunology Division Director and Keynote Speaker, Damien Chaussabel, PhD, discussed new ways of assessing the health of the immune system to help in the prevention and treatment of diseases, specifically tailored to the individual. Elizabeth Mosley, BRI research participant, told the capacity crowd about her struggle with rheumatoid arthritis and why she decided to participate in a BRI clinical trial.

Thank you to the sponsors, donors, volunteers and Emcee, Steve Raible, KIRO 7 News Anchor, for supporting Illuminations and autoimmune disease research.

Diabetes Awareness Day Lights Landmarks Blue

The Pacific Science Center arches were lit blue on Nov. 14 to recognize World Diabetes Day. The iconic arches were among many world landmarks, including the Empire State Building, Sydney Opera House, the London Eye, Leaning Tower of Pisa, Tokyo Tower, and Niagara Falls to be illuminated blue to raise awareness for diabetes. The Puget Sound World Diabetes Committee, including Benaroya Research Institute, also interviewed families with diabetes at the Seattle Center and invited the community to wear blue, the official color representing diabetes.



Life Sciences Research Weekend Brings Science to Life

Benaroya Research Institute, Northwest Association for Biomedical Research and 11 other organizations provided interactive exhibits that allowed visitors to experience hands-on science during Life Sciences Research Weekend at the Pacific Science Center, Nov. 4 - 6. This event provided an opportunity for the community to learn more about the exciting world of life sciences and the key role research plays in our daily lives.



BRI volunteers Mary Roy, Lindsey Castle and Gladys Doronio, discuss BRI research at Life Sciences Research Weekend at the Pacific Science Center.

BRI volunteers were available all weekend to share the latest discoveries and demonstrated the importance of DNA and genes in our daily lives. Tommy T Cell, BRI's superhero, helped explain the important role of regulatory T cells, how they control the immune system and how they can defeat harmful cells.

Learn About the Latest Research at BRI 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, a laboratory tour led by scientists and discussion with board members and other guests.



Damien Chaussabel, PhD, introduces visitors to his laboratory.

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

New Scientist Brings Additional IBD Expertise to BRI

Benaroya Research Institute welcomes Elisa Boden, MD, Senior Postdoctoral Research Associate at BRI and Clinician at the Digestive Disease Institute at Virginia Mason Medical Center. Dr. Boden specializes in inflammatory bowel disease (IBD) both as a gastroenterologist and as a scientist.

“In IBD, the immune system attacks the intestines, causing inflammation,” she explains. “I’m studying how IBD is triggered and why the regulatory T cells that should protect the intestines from inflammation aren’t working. We want to see if we can dampen the immune response and/or boost the response of regulatory T cells to eliminate this disease. In health, the gut maintains a tight balance of the immune system and we need to find a way to restore that in patients with IBD.”



Elisa Boden, MD, brings clinical expertise to IBD research.

As a researcher and a clinician, Dr. Boden has “the best of both worlds. I have the opportunity to interact with patients, usually from a young age, and build a relationship with them over many years. I can understand from a clinical perspective the great need for better research and the questions that need to be addressed to provide the best patient care. As a scientist, I can work to answer those questions and help find more effective treatments.

“BRI is unique in having clinical, translational and laboratory research alongside the expertise of patient treatment at the Digestive Disease Institute,” she says. Dr. Boden recently completed a clinical and research fellowship in IBD at Mt. Sinai Hospital in New York. She received her medical degree from the University of Chicago Pritzker School of Medicine which also has a strong history of IBD treatment and research.

For more information on IBD visit BenaroyaResearch.org.

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(continued from front cover)

- to understand how regulatory T cells fail to control inflammation in IBD. He also collaborates with other investigators at BRI to understand how genetic risk factors for IBD can influence how immune system cells communicate with each other through cytokines.
- Elisa Boden, MD, a new Senior Postdoctoral Research Associate at BRI and clinician at the DDI, is funded through a grant from the Crohn’s and Colitis Foundation of America to study defects in T cell immune regulation in a model of colitis. She also studies novel therapeutics for IBD that target the T cell receptor in humans. (See more on Dr. Boden in “Researcher in the Spotlight.”)
- Jane Buckner, MD, Director of BRI’s Translational Research Program, examines how genes associated with autoimmunity lead to disease. Recently her group has demonstrated how one gene associated with both IBD and Type 1 diabetes, PTPN2, alters the function of immune cells.
- Steven Ziegler, PhD, Director of BRI’s Immunology Research Program, studies thymic stromal lymphopoietin (TSLP), a factor that regulates immune responses at barrier surfaces such as the gut and has decreased expression in IBD. Florence Roan, MD, PhD, Infectious Disease Research Fellow, has shown that loss of this protein leads to more severe inflammation in system models of IBD. She is now exploring how TSLP expression correlates with markers of IBD risk or disease activity in IBD patients, in collaboration with Dr. Lord.
- Dan Campbell, PhD, Principal Investigator in BRI’s Immunology Research Program, studies how a group of immune cells known as regulatory T cells are generated and function to prevent autoimmune and inflammatory diseases like IBD.

Listings of other IBD trials, including participation in BRI’s biorepository program, can be found on the BRI website, BenaroyaResearch.org.

Invite BRI Speakers Bureau to Your Event

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 highly-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.



Jessica Muffet, Speakers Bureau volunteer.

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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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