FALL 2010

BENAROYA RESEARCH INSTITUTE AT VIRGINIA MASON

UNLOCKING THE IMMUNE SYSTEM®

NEWSLETTER

Vol. 2, No. 3

BRI THROUGH THE MICROSCOPE

BRI Celebrates 25 Years of Molecular Medicine Research

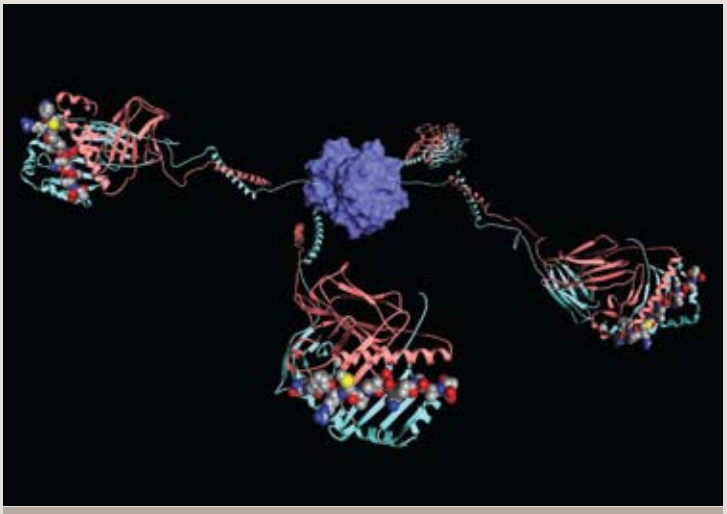
Twenty-five years ago, Virginia Mason Medical Center leadership and the Virginia Mason Research Center (now Benaroya Research Institute at Virginia Mason) board made a momentous decision. They chose to put the resources of the research center toward a new vision — the emerging field of immunology and molecular medicine research. The new programs began in 1985 with the recruitment of Gerald Nepom, MD, PhD, BRI Director, supported in large part by funding provided by the Weyerhaeuser family and friends.

The programs have grown into a world-renowned research institute, with funding volume in 2009 of $28.7 million and a team of more than 200 scientists and staff. The Immunology Program launched in 1985, was followed by the Diabetes Research Program in 1987, the Clinical Research Program in 1991, the Hope Heart Program in 2004 and the Translational Research Program in 2006.

"BRI has kept its focus and retained and recruited very talented scientific leaders over quite a long period of time," notes Dr. Nepom. "This undoubtedly is a major part of the reason we have become recognized as leaders in the field." BRI established its leadership through new discoveries, strategic direction, and organizational coordination on a national and international scale.

Throughout its rapid evolution, BRI's mission has remained the same — to find causes and cures for diseases to improve people's lives. Molecular medicine research has contributed significantly toward this goal. "Molecular medicine in immunology developed as the outgrowth of two converging themes: The understanding that therapies specifically directed at single molecules or pathways can be more effective and less toxic than general immunosuppression, and the understanding that an individual's genetics influence disease course and perhaps choice of therapy," says Dr. Nepom. "The next 25 years will see new and approved therapies from this research.

"As our history relates, it is the combination of community leadership, research supporters, medical opportunities and talented scientists and staff that enable the successful translation of laboratory science to people throughout the world." BRI will hold an international scientific symposium in October to highlight recent discoveries and discuss the future of immunology research.



Computer generated illustration of a tetramer, a pioneering biomarker developed by BRI to detect and measure specific immune cells in blood samples. They are now widely used to improve diagnosis and treatment of a broad variety of diseases.

DID YOU KNOW?

Immune Tolerance Network Celebrates 10th Anniversary

The Immune Tolerance Network (ITN) is celebrating its 10th anniversary. The ITN is a large international clinical research network founded by the National Institutes of Health, with additional support from the Juvenile Diabetes Research Foundation. The ITN is working to establish new treatments for diseases of the immune system. Gerald Nepom, MD, PhD, Director of BRI, also serves as Director of ITN. "The ITN's novel network approach can speed discoveries, increase clinical trials and improve outcomes," says Dr. Nepom.

ADVANCING CURES AND TREATMENTS

25 Years of Molecular Medicine Research

Throughout BRI's 25 years of molecular medicine research, many key discoveries have accelerated the pace to understand autoimmune diseases and find ways for early diagnosis, cures and eventually prevention. Some of the advances include:

- Identification of genetic markers for disease susceptibility, particularly autoimmune (Type 1) diabetes and rheumatoid arthritis.
- Creating methods to generate regulatory T cells in the laboratory that open the door for novel therapies for autoimmune diseases.
- Identification of a triggering cytokine that promotes asthma and other allergic diseases.
- Dissecting the molecular mechanisms for defective DNA repair pathways, an important control point for cancer susceptibility.
- Descriptions of immune system genes that provide insight into the way the immune system evolves and functions.
- Diabetes clinical trial leadership, including pioneering work on insulin formulations, insulin pump systems, human islet transplantation, and immunotherapy for autoimmune diabetes intervention and treatment.
- Production of MHC tetramers — groundbreaking biomarkers to detect and measure specific immune cells in blood samples. They are now widely used to study allergies, vaccination, and autoimmune diseases.
- Pioneering research approaches to rheumatologic disease, from prediction of rheumatoid arthritis to the use of autologous stem cell transplantation for scleroderma.
- Descriptions of novel molecular mediators of cell adhesion and trafficking that underlie inflammatory pathways in immune-mediated diseases and vascular inflammatory states.
- Characterization of molecules in tissues that interact to form a matrix that initiates and regulates a variety of key parameters, controlling cell growth and function.

CLINICAL TRIAL PARTICIPANT

Grant Helps Alaskans Participate in Research

On April 27, 2009, Ben Johnson visited a chiropractor in Juneau, Alaska, for a pain in his hip. Three days later, he was at Virginia Mason Medical Center (VM) in Seattle, receiving radiation therapy for a cancerous tumor on his hip. Ben and his wife, Bertina, travel to Seattle for treatment because there is limited access to cutting-edge medical care and research in their hometown of Hoonah and the surrounding area.

After receiving radiation treatment at VM for the disease, Ben's doctor, Jacqueline Vuky, MD, VM cancer specialist and BRI clinical researcher, told him about a clinical trial at Benaroya Research Institute for a medication that curbs the growth of new blood vessels in tumors. The Johnsons decided to participate in the trial to help others affected by cancer.

Once a month, the Johnsons travel from Hoonah to BRI to participate in the clinical trial. They take a three-hour ferry ride or fly to Juneau and then fly to Seattle. Their travel schedule is long and tiring but they believe Ben's involvement in the clinical trial has been extremely valuable.

Bertina and Ben Johnson travel from Alaska to Seattle for Ben's cancer treatment.

The Johnson's travel to BRI and VM is made possible by a grant from the Rasmuson Foundation of Anchorage, Alaska. The foundation provided BRI with $1 million to bring education and access to clinical trials to Alaskans suffering from a variety of diseases. This supplements the health care of individual providers and agencies already serving patients in Alaska. The generous grant covers airfare, ground transportation and lodging for eligible Alaskans who wish to participate in clinical research trials being conducted at BRI.

For more information about clinical trials and the Rasmuson Grant at BRI, please visit BenaroyaResearch.org/alaska-outreach-program.

FUNDING MEDICAL ADVANCEMENTS

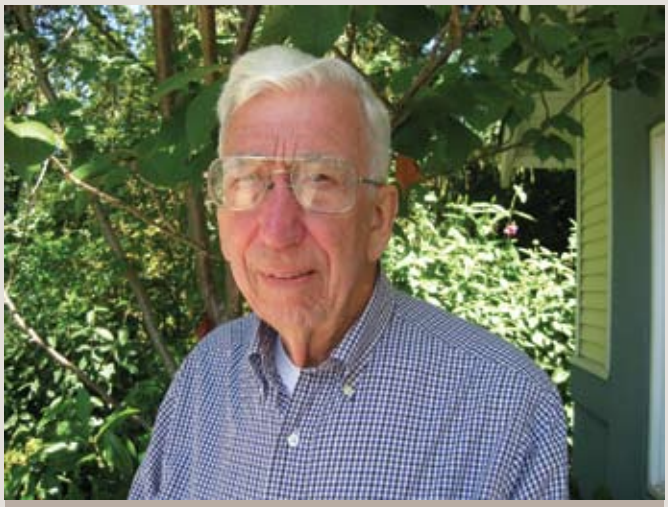
Jack Wimpress, Donating to Find a Cure for Type 1 Diabetes

Jack Wimpress understands diabetes better than most people, because he and his wife, Doris, raised three children with Type 1 diabetes, not only a statistical anomaly, a significant challenge. In the 1950s and 1960s when the children were young there was limited knowledge about the disease. So Jack, as an engineer, and Doris, as a nurse, combined their expertise to support their children. They used a slide rule to calculate how much of each food group should be served, and planned carefully for when each child should be fed. The kids had three measured meals and three measured snacks daily.

Despite the challenges, thanks to Jack and Doris' diligence, the family was very active in traveling, skiing, hiking, and boating.

In the 1960s the couple learned about Benaroya Research Institute's (formerly Virginia Mason Research Center) focus on diabetes and they became very interested. Eventually Jack was invited to join the original research board, which he did enthusiastically, and served for more than a decade. One of Jack's insights as an engineer was that diabetes is a feedback loop problem and something might be gained from analyzing this loop. Interestingly enough, today this is a highly recognized model for researching diabetes.

Jack and Doris (who passed away in 2009) have been connected to BRI ever since. Their first-hand experience with diabetes



Longtime BRI friend and donor, Jack Wimpress

inspired them to financially support BRI's work in diabetes research, which they have done for more than three decades, investing generously to battle this disease that has impacted their family. Their greatest wish is that their grandchildren, who also live with diabetes, will have the hope of a cure.

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

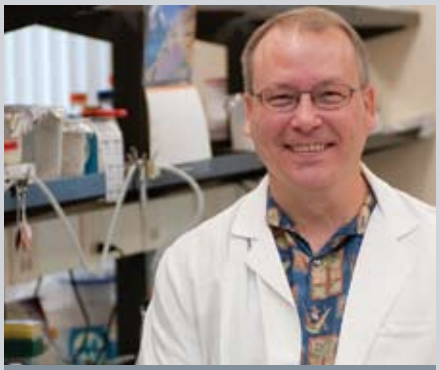
GRANT NEWS

BRI Receives $11.7 Million to Study Lung Infection

Benaroya Research Institute received an $11.7 million federal research grant from the National Heart Lung and Blood Institute of the National Institutes of Health. The grant will bring together key researchers with different, but complementary, specialties to look broadly at the regulation of lung inflammatory diseases. Steven Ziegler, PhD, Program Director for the grant and Director of the Immunology Program at BRI, will lead the team of researchers from BRI and the University of Washington. The scientific program has great potential for improving the health of critically ill patients in the U.S. and internationally.

These diseases, also called pulmonary inflammation diseases, have a tremendous impact on people throughout the world and can lead to serious illness and death. They include influenza, pneumonia, chronic bronchitis, tuberculosis, and HIV/AIDS related respiratory illnesses. Recent emerging lung infections include avian influenza and severe acute respiratory syndrome (SARS). Of great concern is that some of these infections can lead to pandemics. They can also lead to asthma.

"Our goal is to understand what drives the inflammatory response to lung infections, and then learn how best to control that response to eliminate the associated pathology," says Dr. Ziegler. "This new program is unique in that we are bringing great experts in various areas of lung biology to work together. Our program will include four individual projects that probe different, yet complementary and sequential processes of this inflammatory cascade."



Steven Zeigler, PhD, BRI Immunology Program Director, will lead the program to research pulmonary inflammation.

For more information, visit Benaroya Research.org.

2010 Boeing Classic Brings Awareness to BRI and Autoimmune Diseases

The 2010 Boeing Classic, the annual PGA Tour Champions event, held on Aug. 23 – 29, was a huge success with more than 78,000 spectators. Benaroya Research Institute was a beneficiary of the event. The winner of the tournament was Bernhard Langer and the other headliners included golf legends Fred Couples, Tom Kite, Mark O'Meara, Fred Funk, Nick Price and 2009 Boeing Classic Champion Loren Roberts.

The first annual Walk to Unlock the Immune System benefiting BRI was held at the Snoqualmie Ridge Golf Course on Saturday, Aug. 28. The walkers enjoyed the spectacular surroundings of Snoqualmie Ridge, while playing a part in finding a cure for autoimmune diseases.

To help end the first day of Boeing Classic tournament play on Aug. 27, The Golf Club at Newcastle hosted the second annual Grapes on the Green event including wine tasting and a live auction. The evening was a wonderful way to kick-off the final weekend of the tournament and to promote the work BRI is conducting to eliminate autoimmune diseases.

BRI brought together some of its community partners — the Multiple Sclerosis Society, Juvenile Diabetes Research Association, the Crohn's and Colitis Foundation, Lupus Foundation, Spondylitis Society of America, Pat's Fund, Platelet Disorder Support Association, Arthritis Foundation and American Diabetes Association — to help illustrate the connection between the more than 80 autoimmune diseases. Visitors to the BRI tent learned that autoimmune diseases share common mechanisms when the immune system makes a mistake and attacks healthy cells.

Leaders of the Walk to Unlock the Immune System included Jack Nagan, BRI Executive Director; Gaylia Meitzen; Cindy Klapperich; BRI's new T Cell mascot; Trish Markey; and Gerald Nepom, MD, PhD, BRI Director.

The Boeing Classic also included events such as the Seahawks Rumble at the Ridge, The Boeing Classic Youth Clinic featuring Champions Tour Professional Jeff Sluman, and the Korean Air Pro-Am.

"We want to thank all the spectators, volunteers, golfers and partners that helped make the 2010 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." For more information, visit BoeingClassic.com.

BRI Triathlon at Seafair, Expo and Open House – A Great Success

The BRI Triathlon Expo and Open House was a great success! On Saturday, July 17, approximately 120 athletes, community members and neighbors toured the BRI building and listened to presentations given by BRI scientists John Gebe, PhD, Robert Vernon, PhD, and Eddie James, PhD. BRI tour guides led groups through the first floor labs and handed out BRI information at the Expo on Ninth Avenue.

On Sunday, July 18, nearly 2,000 competitors participated in the Benaroya Research Institute Triathlon at Seafair. The course at Lake Washington consisted of a half-mile swim, 12-mile bike ride and 3.1-mile run. The first place finisher, Rusty Pruden, set a course record with a time of 57 minutes, 5 seconds. BRI staff handed out information at the BRI booth. The event benefited autoimmune disease research at BRI.

Bob Vernon, PhD, Principal Investigator at BRI, Hope Heart Program, discussed islet cell research with the Open House participants.

BRI Uses Computing and Information Technology to Accelerate the Study of the Human Immune System

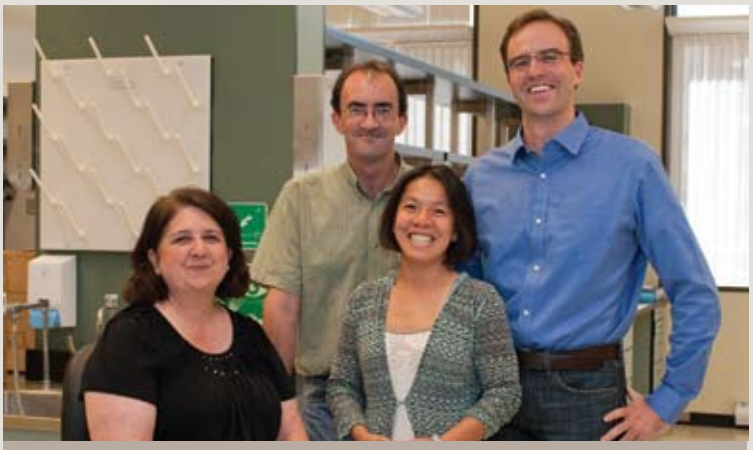
With the explosion of data from genome studies and molecular profiling technologies, huge amounts of biological information are now available. How to use this information to advance medicine and improve care for people with autoimmune or immune-mediated diseases is more challenging.

Benaroya Research Institute is solving this problem by launching a new division called Systems Immunology. Damien Chaussabel, PhD, serves as Director and Charlie Quinn leads the development of Data Management technologies. Dr. Chaussabel is formerly Associate Investigator and Core Director, Baylor Institute for Immunology Research, and Director, Center for Personalized Medicine, Baylor University, Dallas. Charlie is President of Onverra Software and was responsible for Informatics at Baylor Institute for Immunology Research.

"The goal of the program is to study molecular profiles in humans to assess the status of their immune systems and use this information for the early detection of disease complications or response to therapy," says Dr. Chaussabel. "We will study all of the components of the immune system in all of their complexity. We will monitor change for tens of thousands of parameters simultaneously and use the information to better understand diseases and how to treat them." This new approach supports the goal of personalized medicine — finding the best course of diagnosis and care for each individual person.

The Systems Immunology approach brings high throughput profiling technologies and bioinformatics to assist all of the science programs at BRI. "It will rely on cutting-edge technology but also continuously explore novel avenues for exploiting massive amounts of data that we and other groups are generating," says Dr. Chaussabel. "It will also be very collaborative. It will serve as a platform supporting a wide range of projects at BRI but also reach out to collaborators in Seattle and beyond."

At Baylor, Dr. Chaussabel and his team pioneered studies using bioinformatics in immunologic diseases. He developed a thriving genomics and bioinformatics team of immunologists, molecular biologists, bioinformaticians, software engineers and biostatisticians. "The main focus for all these years has been patient blood profiling, with several key papers demonstrating the value of this approach for the study of autoimmune and infectious diseases. We also published resource papers where we describe novel strategies for the mining of these types of data. We started expanding the program to cancer and transplantation. We also acquired a lot of expertise measuring responses to vaccines and to biologic drugs. There are several exciting projects that are coming down the pipeline and that we plan to publish soon."



The new Systems Immunology team includes Vivian Gersuk, Genomics Core Manager; Charlie Quinn, developer of BRI's new Data Management Systems; Quynh-Anh Nguyen, Research Technician; and Damien Chaussabel, PhD, Associate Member and founder of BRI's new Systems Immunology research efforts.

As a key example of how this work benefits patients, Dr. Chaussabel and his team used systems immunology in the development of biomarkers and identification of therapeutic targets. "Applying high throughput profiling technologies in the context of human studies really makes an impact," he notes. "The autoimmunity program led by Virginia Pascual, a colleague I have worked very closely with at Baylor, is the perfect example. High throughput molecular profiling of systemic onset juvenile arthritis and systemic lupus has led to novel therapeutic modalities and transformed the life of many of her patients."

"The six years we have spent at Baylor have been incredible and the program there is very successful," says Dr. Chaussabel. "Building a program at BRI is a new challenge, but it's an exciting opportunity to work with many collaborators to find innovative solutions to difficult problems."

"While we have made many discoveries and created many applications and utilities during that time, we have the sense that we are only just getting started and are looking forward to moving to the next level in Seattle and at BRI," noted Charlie Quinn.

UPCOMING EVENTS

Step Out With BRI to Fight Diabetes Oct. 9

The American Diabetes Association's 2010 Step Out – Walk to Fight Diabetes will be held throughout the Northwest on Saturday, Oct. 9. The 2 or 5 mile walks will take place in Seattle at Magnuson Park, Point Defiance Park in Tacoma and in Eugene, Ore.

The BRI Diabetes Clinical Research Program will be at these events offering TrialNet screening via test kits, information on BRI and details on the latest diabetes clinical trials. For more information on the 2010 Step Out – Walk to Fight Diabetes, please visit http://stepout.diabetes.org.

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.

Seattle-Sweden Diabetes Awareness Day Oct. 16

U.S. and European researchers will share the latest research in Type 1 diabetes with the public at this event. Gerald Nepom, MD, PhD, Director of BRI, and Carla Greenbaum, MD, Director of BRI's Diabetes Research Program, will speak. BRI will also conduct TrialNet screening. For more information, visit www.jdrfnorthwest.org.

Local Research at the Pacific Science Center Nov. 5 – 7

The 4th annual Life Sciences Research Weekend of the Northwest Association for Biomedical Research will be held November 5 - 7 at the Pacific Science Center in Seattle. BRI and other local research organizations will host hands-on activities that reflect the innovative life sciences research they are conducting. For more information, visit Benaroya Research.org.

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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