



Advances in Immunology Bring Hope for People with Autoimmune Diseases

Gerald Nepom, MD, PhD, Director of Benaroya Research Institute at Virginia Mason (BRI) and the Immune Tolerance Network (ITN) describes the future of immunology research.

What do you foresee as the future of immunology? There is no organ system or major disease that is not impacted by the immune system. Increased understanding of the immunological impact on health will inevitably lead to integrating immunological perspectives into medical practice on a broad scale.

Can you give some examples of what specifically may be achieved? One of the best examples—and it is already happening—is the growing understanding of the role of inflammation in diseases that were previously thought to be something else. Examples include progression of atherosclerotic plaques, certain stages of Alzheimer's, the enhanced ability of a cancer to metastasize and many more. Advances can be made by treating inflammatory components of many of these common diseases. In another area, a growing number of autoimmune diseases are now being treated in clinical trials using powerful immunomodulator drugs and molecules that have come from laboratory discoveries in the last two decades. Another area is the development of vaccines for some of the remaining epidemics, such as malaria and tuberculosis. There have been many notable successes, so this is not only a hope for the future, but success for today.

What will be the future in the lab? More informatic tools and more computing power mean that immunological profiling will become an individualized medical activity. This will be a very important component of personalized medicine.

What will be the future in clinical trials? Because the immune system is complex and has evolved redundant pathways over millennia in response to diverse challenges, we are very likely going to need to treat immune dysfunction with combinations of drugs. This is going to take time, since in our current regulatory environment, each therapy is first tested individually before proceeding to combinations in trials. Nevertheless, I think combination immunologic therapy will become a powerful medical option.



More than 400 scientists attended the Immunology: Looking Forward symposium. BRI held the event to celebrate 25 years of molecular medicine research and to share ideas to accelerate advances in immunology. Bart O. Roep, MD, PhD, Head of the Division of Autoimmune Diseases at Leiden University Medical Center, Leiden, Netherlands, and Jane Buckner, MD, BRI's Director of the Translational Research Program, both spoke at the symposium.

What do you see as BRI's contribution to the future of immunology? We were one of the first institutions to adopt a sole focus on this area of biomedical research. By creating ways to translate findings from the lab into clinical studies, we are very well positioned to conduct pilot studies to address some of the most challenging questions in the field.

What do you see as ITN's contribution to the future of immunology? The ITN has tremendous resources available to conduct clinical studies of the best and most challenging concepts that come from immunologists all over the world. The ITN expects to increase both the speed and quality of trials evaluating new immunological therapeutics.

Bioinformatics – New Tools to Understand Diseases

In the past, when scientists completed an experiment, they would analyze the results and publish any noteworthy discoveries. Then the data would be filed away.

Today, with the availability of cutting-edge molecular profiling tools, vast amounts of data are generated very quickly. Accumulating and analyzing this data can prove extremely valuable to answer new questions and probe for novel discoveries. The emerging field that focuses on the exploitation of this tsunami of data is called “bioinformatics.” Bioinformatics uses mathematics, information technology, computational and statistical techniques and theories to manage and analyze biological data. BRI launched a new bioinformatics group within its Systems Immunology division in September.

“At BRI, our bioinformatics area encompasses several goals,” says Damien Chaussabel, PhD, Director of BRI’s Systems Immunology. “The first is data management. We want to collect and safeguard the research data with the highest levels of integrity. Our database includes a broad range of analyses of human blood samples and serums in health and disease. This information is extremely valuable for scientific discovery.”

The second goal is to provide accurate data analysis. “The data is so complex that you need numerous specialists to interpret the data correctly,” says Dr. Chaussabel. “The team may include clinicians, immunologists, molecular biologists, bioinformaticians, software engineers and biostatisticians. Together they can collaborate to interpret the data in a fruitful manner.”

The third is to create ways to make the data easily available to scientists. “For instance, if a scientist is interested in a specific gene and its effect on the immune system in a particular disease, he or she can explore our database and see how this gene plays a role in health and disease.” Charlie Quinn, BRI’s head of Data Management Technologies created a “Gene Expression Browser” that allows researchers to look at gene expression across a variety of studies. “Bioinformatics allows us to preserve biological research and use it for future work in a quicker, more cost effective way,” notes Dr. Chaussabel. For more information, visit BenaroyaResearch.org.

Joining the BRI Registries Helps Scientists

Nicolette Athis is well aware of autoimmune diseases. Maureen Tverberg, Nicolette’s partner, has Type 1 diabetes and other members of Maureen’s family are affected by autoimmune diseases. Nicolette wanted to help find a cure for these devastating diseases, but did not know how to make a difference.

While participating in the Benaroya Research Institute Triathlon at Seafair, BRI’s mission of finding the causes and cures for autoimmune diseases appealed to Nicolette. She learned about the Translational Research Program that coordinates registries of blood and tissue samples, medical histories and other data that are used in research at BRI. The registries include people with autoimmune diseases and other immune-mediated diseases such as allergy and asthma. BRI also maintains a registry of healthy people for comparison purposes. Even though Nicolette does not have an autoimmune disease, she can be a part of the registry and help scientists understand how healthy immune systems work as compared to those with diseases.



Maureen and Nicolette – long-time participants in the BRI Translational Research Program.

The Translational Research Program acts as an interface between the laboratory researchers, clinicians and patients. The program enhances communication between clinicians and scientists as well as providing the resource of the immune system registry and repository to scientists both at BRI and elsewhere.

For the past six years, Nicolette has been donating samples to BRI. Maureen has also joined the registry. About every three months, Maureen and Nicolette are asked to give their blood samples. The samples are added to the registry and are used in various research projects. Nicolette believes she has found a way to make a difference in ending autoimmune diseases and contributing to groundbreaking research.

To learn more information about the Translational Research Program or clinical studies, please visit BenaroyaResearch.org/clinical-trials/research-studies/study/268.

Family and Friends Honor Marta Connell by Donating to BRI

Every fall on the first Saturday after Labor Day you will find Steve and Terri Ann Wehmeyer out on the Carnation Golf Course, with 60 to 70 of their family and friends. They're hosting a reunion of sorts, which includes golf, dinner, poker runs and prizes. They are having a great time, but there is a purpose to this fun, as they are honoring a very special person, Marta Connell. Ten years ago, Marta—Terri Ann's oldest sister—died at the age of 39 from primary pulmonary hypertension.

After losing Marta, Terri Ann and her husband Steve wanted to do something to honor Marta and to fight back against this disease. They decided to start a family and friends golf tournament. Their friend, Chad Tachell arranges for the use of the golf course and other friends donate the prizes. To date they have given more than \$40,000 to Benaroya Research Institute to support research efforts focused on pulmonary disease.

What's amazing is that their enthusiasm and passion ten years later is as strong as ever. They have now added a dinner cruise to their festivities, selling tickets to a luxury cruise hosted by their friend Captain Bob. By supporting research they are investing in the future of others, while keeping Marta's memory with them in a most tangible way.

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



Marta Connell and her sister Terri Ann Wehmeyer. The Wehmeyers, along with friends and family, honor Marta with events that contribute to BRI's research.

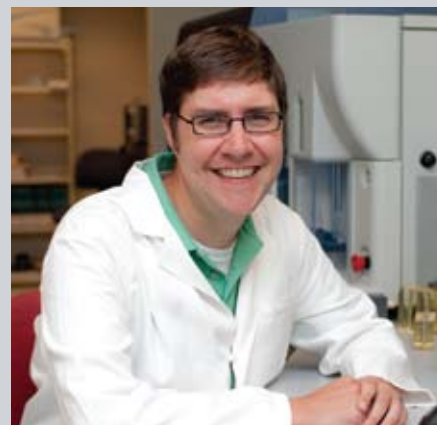
BRI Receives \$2.2 Million to Study Critical Factor in Autoimmune Diseases

BRI received a \$2.2 million federal research grant from the National Institute of Allergy and Infectious Diseases at the National Institutes of Health to investigate a key factor that plays a critical role in preventing autoimmunity and limiting immune-mediated inflammation. If scientists can find a way to manipulate or program this factor, it can be used in cellular therapy to help eliminate these diseases. This particular grant focuses on diseases such as persistent mycobacterium tuberculosis infection, psoriasis, rheumatoid arthritis, Type 1 diabetes and multiple sclerosis.

"Autoimmune and immune-mediated diseases are a major public health challenge," says Daniel Campbell, PhD, Associate Member at BRI and Principal Investigator for the grant. "The immune system is like a finely-tuned engine. It works to eliminate bacteria, viruses and other

infectious threats to our bodies. But sometimes it overreacts or underreacts. In this grant, I'm studying a particular type of cells that help maintain this balance and turn off the immune system when it overreacts. If we can understand how these cells put the brakes on the immune system, and how their activity is controlled during infection and autoimmunity, we may be able to develop individual therapies to help each patient with his or her specific disease situation."

For more information on this and other grants, please visit BenaroyaResearch.org and click on News and Press Releases.



Daniel Campbell, PhD, is Principal Investigator for the grant award to study a key factor, T-Bet, that plays a critical role in preventing autoimmunity and limiting immune-mediated inflammation.

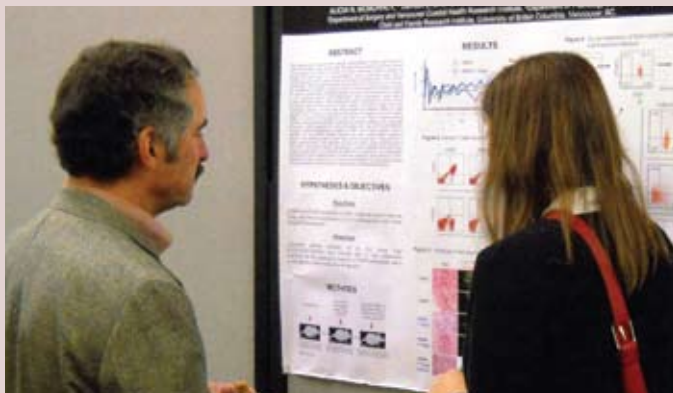
BRI Symposium Attracts Scientists

More than 400 people attended the immunology research symposium, *Immunology: Looking Forward* presented by Benaroya Research Institute at Seattle's Town Hall on Oct. 27 - 28. To celebrate the 25th anniversary of the immunological program at BRI, the institute invited top scientists in the field to Seattle to examine and discuss recent discoveries. The keynote presenter, Jean-Laurent Casanova, MD, PhD, of The Rockefeller University, gave a lecture entitled *Infectious Disease: Inborn Errors of Immunity?* Other lectures included: *Toward Personalized Immunotherapy of Cancer* by Brad Nelson, PhD, *Pregnancy Malaria: A Vaccine Designed by Nature* by Patrick Duffy, MD, and *Achieving Tolerance in Autoimmune Diabetes - Challenges and Opportunities* by Jeffery Bluestone, PhD.

Thank you to the presenters, attendees and sponsors who made this event a huge success. Sponsors included: ZymoGenetics, Miltenyi Biotec, Invitrogen, Immune Tolerance Network, Novo Nordisk, Full Spectrum Cell Analysis, eBioscience, BioLegend, Adaptive TCR Technologies, Lab Performance Specialists, Genentech, Biogen Idec, and the Institute of Translational Health Sciences.



David Rawlings, MD, Director, Center for Immunology and Immunotherapies, University of Washington, Seattle, addressed an approach to understanding autoimmune diseases.



Gerald Nepom, MD, PhD, Director of BRI, discusses research poster presentation with symposium scientists.

Children Learn About Life Sciences at the Pacific Science Center

The Life Sciences Weekend at the Pacific Science Center, Nov. 5 - 7, 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. More than 1,500 children and adults attended the event.

Benaroya Research Institute, Northwest Association for Biomedical Research and 11 other organizations provided interactive exhibits that allowed visitors to experience hands-on science. BRI volunteers were available all weekend to share the latest discoveries and used interactive workbooks to help children understand autoimmune diseases. Tommy T-Cell, BRI's superhero, helped explain the important role of regulatory T-cells and how they control the immune system and can defeat harmful cells.



Tommy T-Cell, BRI's regulatory T-cell superhero, with BRI volunteers during Life Sciences Weekend at the Pacific Science Center.

5th Annual Seattle-Sweden Diabetes Awareness Day

An enthusiastic and passionate crowd gathered at the Microsoft campus on Oct. 16 for the 5th Annual Seattle-Sweden Diabetes Awareness Day. The goal of the event was to increase awareness about Type 1 diabetes and provide an opportunity for the lay public to ask questions, and interact with leading experts in the field. Sweden and Seattle have an unusually high percentage of children with Type 1 diabetes.

Television and radio personality, Pat Cashman, moderated the discussion that covered topics such as: *What Triggers Diabetes in Children?*, *The Artificial Pancreas* and *Is It Possible to Prevent Type 1 Diabetes?* BRI Director of the Diabetes Research Program, Carla Greenbaum, MD, presented on *Saving Beta Cells*. For more information about diabetes research at BRI, please visit BenaroyaResearch.org/disease-information/disease-research/diabetes.

James Dennis, PhD, and Team Bring New Tissue Bioengineering Skills to BRI

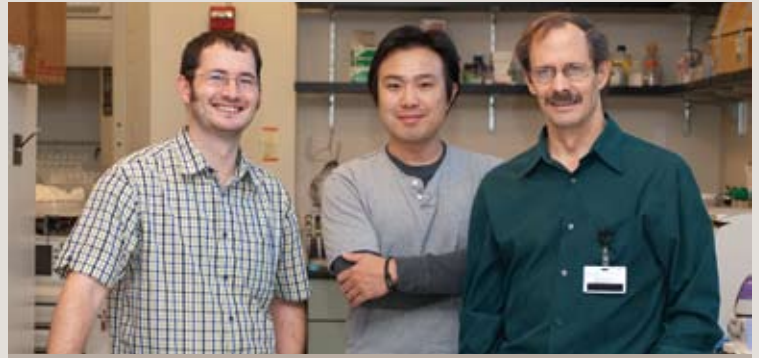
It's like a tale out of science fiction—bioengineering cartilage to repair joints and other areas of the body. But it's being done today. James Dennis, PhD, an expert in mesenchymal adult stem cell biology and tissue engineering, and his team recently joined Benaroya Research Institute. Their work will expand BRI's bioengineering capabilities.

Dr. Dennis is an expert in tissue engineering related to repairing cartilage and making joint cartilage. He also has developed methods to deliver targeted adult stem cells to repair particular tissues. He formerly was Assistant Professor, Department of Orthopaedics at Case Western Reserve University in Cleveland. He also served as faculty in the Department of Biomedical Engineering, Otolaryngology, Head and Neck Surgery, and Pathology, at Case Western Reserve University.

In one of his projects, Dr. Dennis is using a tissue-engineered piece of cartilage, created in his laboratory, to repair the trachea. The goal for clinical application is to create a trachea for infants who are born with tracheal defects, or to repair tracheal injuries for patients of all ages. Dr. Dennis has tested this cartilage in model systems with success. This project is funded by the National Institute of Dental and Craniofacial Research at the National Institutes of Health (NIH). "This study addresses not only the pragmatic issue of repairing a trachea, but delves into how the molecular structure of chondrocytes (cells found only in the cartilage) differs throughout the body."

Another project focuses on repairing joints using large sheets of cartilage to cover the entire surface of the joint. "We're now working on a model for the shoulder joint," he says. "This could be very helpful for patients with arthritis or people who have suffered from an injury to the joint." This work is funded by the National Institute of Arthritis, Musculoskeletal and Skin Diseases of the NIH.

He is also interested in finding ways to send adult stem cells for tissue repair to the tissues of interest. "The body has an amazing ability to repair itself," he notes. "But in the case of major injury or diseases, these repair mechanisms are often insufficient. Our goal is to send targeted stem cells to the affected tissues to help repair them." Dr. Dennis and his team have developed cellular "paints" that attach themselves to cell membranes and bind to the tissue of interest. He has two grants in this area, one from the National Institute of Arthritis and Musculoskeletal and Skin Disease of the NIH



The Dennis Laboratory includes Thomas Kean, PhD, and Hisashi Mera, MD, PhD, both postdoctoral fellows, and James Dennis, PhD. Graduate student Adam Whitney will be joining the team in January.

and one through the Department of Defense. Dr. Dennis and colleagues have founded Cell Targeting, Inc., to further develop this work.

Dr. Dennis works with Margaret Allen, MD, within BRI's Hope Heart Program as well. She is interested in using this technology in her five different grants for muscle repair, two for heart repair after heart attacks, and three for skeletal muscle repair after major traumatic injuries. "We're researching how to grow new heart muscle cells. Dr. Dennis' work is integral to this goal since the addition of mesenchymal stem cells may help improve the blood supply to the heart muscle grafts and enhance the survival of new muscle cells," she says. She is also investigating how to repair significant loss of muscle mass that occurs in some industrial or auto accidents or on the battlefield. "We're making use of a population of stem cells that occur naturally in skeletal muscle to help speed up the process of skeletal muscle repair."

Dr. Dennis joined BRI because of its excellence in immunology. He is interested in expanding his work in inflammatory bowel disease, arthritis and other areas of immunology. "We can use the body's immune system to learn how to protect cells from injury and to control the inflammatory response," he says. "I'm very excited to become part of the research team here at BRI."

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.

Announcing Benaroya Research Institute Speakers Bureau

Schedule BRI's Speakers Bureau to Speak to Your Group

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, an interesting and informative PowerPoint presentation, 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) 341-1345.



Judi Rising, BRI board and speakers bureau member, speaking at a Virginia Mason Medical Center event.

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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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