Dear Friends,

I wanted to let you know of some upcoming changes at BRI: I have been working closely with the BRI Board over the last six months to plan for continuity of leadership at BRI, as I intend to step down as director at the end of this year. I will be devoting my time to leading the Immune Tolerance Network (the large international effort to develop and test immune therapies for diabetes, autoimmunity, transplant and allergy), still closely involved with other scientists at BRI. However, institutional leadership and administrative oversight will transfer to Dr. Jane Buckner, who has been selected to be my successor in 2016.

I am very pleased by this choice, which assures that the key focus of BRI on discovering causes and cures for autoimmune diseases will continue, and build. Jane is currently associate director at BRI and has been closely involved with me in both the strategic direction of our work and in implementing many of the most important translational initiatives for clinical applications. Jane is also a highly respected scientist and physician, committed to improving patients’ lives through our research efforts.

Your interest and support of BRI has been instrumental in our success, for which I am very grateful. It has been a privilege to lead BRI’s research programs for the last 30 years, and I look forward to a bright future for the organization.

Best regards,

Jerry

Gerald Nepom, MD, PhD, director of Benaroya Research Institute at Virginia Mason (BRI) and the Immune Tolerance Network (ITN).
For nearly 45 years, Marcia Wollam has cared for people at Virginia Mason Hospital. Initially she served as an LPN and then she became a patient flow coordinator on the Rehabilitation Unit. But she always wanted to do more to help people. She participated in research in the 1970s at Virginia Mason by donating her bone marrow. And as soon as she learned about the Benaroya Research Institute biorepositories, she joined in 2006.

“I wanted to be a part of a larger pool of participants that would eventually lead to something good for many people,” she says. A biorepository, or biobank, consists of blood and tissue samples linked to medical and demographic information collected from people with a specific disease or condition or from healthy volunteers. All of the information gathered is kept confidential, and samples and health information used by scientists are coded with a number. BRI maintains an extensive biorepository with more than 100,000 samples dating back to 2000. The biorepository includes 11 disease categories and one for healthy people. BRI scientists and colleagues collaborate to study this information. They work to understand the nature of disease initiation and progression to better target therapy and look for new therapies.

HOPE FOR THE FUTURE

“I’m hoping that whatever role my samples play, that they further the cause to eliminate disease and reduce delays in getting answers,” explains Marcia. “The more of us that join, the more answers we will get, and the more treatments will become available. Waiting for research to find results for a person’s condition is one of the most frustrating things I can imagine. My husband, Bud, who passed away in 2010, had what’s called an “orphan” disease—not enough people have it to make research worthwhile for companies that try to produce drugs. That was hard for Bud to deal with, and for me too. Hopefully, with this work we can expect progress more quickly.”

Participating is easy, Marcia notes. “There are a few simple consent forms to sign, and the BRI staff members who collect the blood always make themselves available at a time that is convenient for me,” she says. “They are great. They call or send me an e-mail when they need a sample; it takes less than an hour and is relatively painless.

“People who participate are hereby joining the BRI-Virginia Mason collective effort to obtain answers, not just for our patients, but for our own staff and their families too. Not to mention the rest of the world!”

To find out more or to join the biorepository, call toll-free 1-877-202-5200 or contact biorepository@BenaroyaResearch.org. For the diabetes biorepository, call toll-free 1-800-888-4187 or contact diabetes@BenaroyaResearch.org.
T
here are approximately 50,000 immune cells in
every single drop of blood. In a person with an
autoimmune disease, only one or two of those cells
cause the disease, while the others are busy protecting
the body from unrelated infections and toxins. Benaroya
Research Institute is conducting new research to discover
and interrogate these rare, specific cells to improve
diagnosis and therapy of autoimmunity. And by focusing
on these rare disease-associated cells, BRI is learning
the key molecular patterns of the cells in individuals who
have immune-mediated diseases, and those patterns that
determine who responds to treatment.

Over the last few years, several unique and pioneering
technologies at BRI have been combined to create a
“pipeline” approach to find and study these rare cells. The
pipeline begins with identifying the autoimmune-causing
cells in a blood sample, using markers on these cells
that allow researchers to isolate them for study. Cells are
then captured in sophisticated nanofluidic chambers
in equipment that separate the RNA, which holds the code
to the cell’s destiny. Another high technology machine
reads that code using advanced DNA sequencing. (The
nucleic acids, DNA and RNA, carry the genetic information
necessary to build and maintain an organism’s cells and
pass genetic traits to offspring.)

In this fashion, BRI’s scientists can take blood samples
from diverse research study participants—for example,
people with peanut allergy, or children at risk of type
1 diabetes, or patients taking experimental therapy for
rheumatoid arthritis—put the samples into this pipeline,
and discover the underlying disease-associated code that
drives each immune cell.

“It’s an important advance,” says BRI Director Gerald
Nepom, MD, PhD. “Our ultimate goal is to be able to find
the right treatment at the right time for each person. By
understanding the underlying cellular programs that are
present in patients with disease, we can improve diagnosis
and therapy, making significant contributions to ultimately
eliminate autoimmune and other immune diseases.”

BAR CODING T CELLS

When functioning normally, the immune system will seek
out and destroy invaders of the body, such as infections.
But sometimes the immune system goes awry and attacks
the body’s own tissues and causes autoimmune diseases
such as type 1 diabetes, multiple sclerosis or rheumatoid
arthritis. In other cases the immune system overreacts
to a foreign substance and causes an allergy.

The T cells in the immune system are the destructive
leaders in these immune responses. Over the last
decade, BRI scientists have become international
leaders in identifying ways to isolate these rare
and hard-to-find cells.

“Our scientists can look
at specific T cells and
decipher a sort of “bar
code” that distinguishes
each individual T cell from
the billions of other T cells
found in every individual,”
says BRI Director of
Systems Immunology Peter Linsley, PhD. Using these
bar codes, researchers can determine the functions of
individual T cells, what happens to each disease-causing
T cell during disease progression and how it responds to
treatment.

One of the unique features of this BRI analytic pipeline
is the development of bioinformatics tools that enable
researchers to link what single T cells do with what these T
cells are targeting.

IMPACT AND FUTURE POTENTIAL

Knowing what T cells are doing and what they are
targeting is key to being able to apply this technology
to many different types of immune disorders, ranging
from allergy to autoimmune diseases, to vaccines and
even cancer therapy. For example, in the current peanut
allergy and grass allergy clinical trials run by the Immune
Tolerance Network, pipeline analysis by the Wambre and
Kwok laboratories at BRI is being used to try to determine
not only the cellular effects of therapy, but also the type
of variation seen in different people that may explain why
some people respond and others don’t. These studies
are not only uncovering new insights into the causes of
disease, they are also leading the way toward an era of
personalized medicine, in which we will customize therapy
to the right targets in each individual.
As a young, enthusiastic scientist, Jessica Hamerman, PhD, joined Benaroya Research Institute in 2006 ready to delve further into understanding the inflammatory response of a certain type of cell that is an early responder to infections. This inflammatory response is necessary to clear infections, but if it continues unchecked, it can cause problems such as autoimmune diseases or septic shock.

She was passionate about her area of interest and excited to set up her laboratory. However, young investigators can’t get grant funding to start their research because they haven’t generated enough preliminary data showing their ideas are feasible and worth exploring. BRI knew Dr. Hamerman’s postdoctoral work was very promising and offered to provide support to set up her laboratory. The funding came from BRI and anonymous donors and allowed her to buy equipment and supplies to get her lab off the ground.

Several years later, the same donors provided funding over three years to help her continue developing her research. “The donations have helped me immensely,” says Dr. Hamerman. “At first the support helped me get started so I could develop my ideas and provide initial data to the National Institutes of Health and other funding agencies. Later on, I was able to expand my research into other areas and receive additional funding. The environment at BRI is wonderful because you can learn from the other scientists and gain expertise and knowledge.”

She also had the opportunity to meet several times with one of her donors. Although her donors have chosen to be anonymous, they are involved and interested in her progress. “It was a great experience to show him my work and share the advances in our research. He was very curious and I could demonstrate how his funding made advances in scientific understanding.”

Dr. Hamerman is now an associate member at BRI and an affiliate associate professor in the Department of Immunology at the University of Washington School of Medicine. Two graduate students, a postdoctoral student and a staff scientist are learning from her now and on their path to becoming young investigators.

She has broadened her work to look at the inflammatory response in autoimmune diseases in human blood samples from the BRI biorepository. She has discovered several specific proteins that could be targets for therapy to manipulate the immune system to achieve more efficient elimination of infections and to regulate the inflammatory response during autoimmune disease.

These discoveries can be used to help develop vaccines and immune-modulating drugs to prevent and treat infections as well as to regulate inflammatory response during disease. One of her major discoveries is in lupus, a chronic, systemic autoimmune disease that can affect the joints, skin, kidney and other organs of the body. Coincidentally, her grandmother had lupus, so she is always aware of the personal toll of these diseases.

“Donor support outside of grant funding is essential to BRI,” says Dr. Hamerman. “It supports innovative pilot projects, new technology and young investigators. We just can’t thank our generous supporters enough for accelerating the advancement of medicine and science.”

For more information on donating to BRI, visit BenaroyaResearch.org/support-us, call 206-583-6083 or email foundation@virginiamason.org.
THIRTY YEARS OF PROGRESS

In the early 1980s, the leadership team at Virginia Mason made the important decision to establish a biomedical research center focused on immunology. Immunology at that time was an emerging field, anticipating a future era of medical applications. In this brief article, we look back on the last 30 years, reflecting on the role that Benaroya Research Institute at Virginia Mason has played in transforming our understanding of autoimmune and immune-mediated diseases, helping bring numerous new therapies to patients with these and related disorders.

’80S: EARLY SUCCESS

The first step was taken in 1985, with the recruitment of Gerald Nepom, MD, PhD, to lead this transition. For the next decade, BRI (then known as Virginia Mason Research Center) built a reputation as a powerhouse for understanding the genetic contributions to autoimmune diseases, particularly rheumatoid arthritis, type 1 diabetes, multiple sclerosis and celiac disease. BRI led the development and application of new technologies for identifying genes associated with disease susceptibility and performed pioneering studies in which these genes were experimentally manipulated to foster understanding of their function. With this success came recognition—the National Institutes of Health highlighted BRI’s work as one of the cornerstones of arthritis research in the 80’s. It also generated funding—BRI’s external grant funding grew tenfold over the first decade. Finally it brought growth: Several new investigators joined BRI during this era, bringing new insights, technologies and energy to the quest for answers to autoimmune diseases.

Gerald Nepom, MD, PhD, established the Immunology Program 30 years ago. As a scientist and director of BRI and the ITN, he has contributed greatly to progress in autoimmune and immune-mediated disease research. Attending the dedication of the program (L - R) are Kenneth Wilske, MD; Roger Lindeman, MD; George Weyerhaeuser; and Dr. Nepom.

NOW: INTERNATIONAL LEADERSHIP

Development of BRI’s new facility, and its growing international stature, enabled a broader vision, one that recognized the potential for major impact and growth. Steven Ziegler, PhD, Carla Greenbaum, MD, and Jane Buckner, MD, among others, established dynamic programs at BRI that focused on basic immunology, clinical trials and translational research, respectively, including recruitment of additional investigators—with nearly 25 principal investigators now working at BRI, supported by nearly 300 staff.

In the first decade of the 21st century, Benaroya Research Institute

• led the development of targeted patient registries and sample repositories for the study of autoimmune diseases linked to clinical trials of experimental therapeutics;
• became a leader in type 1 diabetes clinical trials that showed it was possible to stop disease progression by interrupting immune mechanisms;
• and continued to discover fundamental new insights into specific genes, molecules, and cells that hold the key to understanding causes and cures of immune disorders.

BRI’s history of leadership in this area of biomedical research is now widely recognized, and BRI investigators are frequently called on to advise other institutions, organize scientific conferences and collaborate on large-scale initiatives for novel therapies. What started as a small program in autoimmune genetics is now a leader of major international programs such as the Immune Tolerance Network and TrialNet. BRI is still committed—as it was in 1985—to the core mission of linking fundamental discoveries in basic immunology with opportunities for medical interventions that improve patients’ lives.

’90S: NEW THERAPIES

In 1991, together with Virginia Mason, BRI recruited Daniel Furst, MD, to lead the clinical research programs, a decision that coincided with the introduction of “biologics”—genetically engineered proteins that mimic natural immune regulation—into clinical trials. BRI became a center for testing new immune modulators in patients with arthritis and other disorders, the beginnings of the Institute’s current emphasis on “bedside to bench” research that bridges the gap between discovery and treatment.

Throughout the 1990s, BRI pioneered the development of tools and concepts that linked autoimmune genes with autoimmune patients. This included detailed understanding—at the molecular level—of how mistakes by the immune system lead to disease. This contributed to a fundamental shift in which immune intervention became a prominent target within the broader scientific community. The BRI Board recognized the opportunities this presented for medical impact, and in the mid-1990s made the commitment that led to the state-of-the-art facility now known as Benaroya Research Institute at Virginia Mason.

BRI’s current building opened in 1999 and was renamed to reflect the generosity of the Benaroya family.
**BOEING CLASSIC GOLF TOURNAMENT**

*What:* The Boeing Classic, an official PGA Champions Tour event featuring the legends of golf 50 years or older, will benefit Benaroya Research Institute.

*When:* Aug. 17–23 at TPC Snoqualmie Ridge

*Contact:* For more information and ticket options, please visit BoeingClassic.com.

**EXECUTIVE WOMEN’S DAY**

*What:* Executive Women’s Day at the Boeing Classic is an opportunity for women business leaders to learn from each other and network in an exclusive and engaging forum. The event includes keynote speaker, Molly Fletcher, a trailblazing sports agent and now a speaker, consultant and author.

*When:* Aug. 18 at TPC Snoqualmie Ridge

*Contact:* For more information and ticket options, please visit BoeingClassic.com/exec-womens.

**GRAPE ON THE GREEN**

*What:* Join us for wine tastings from premier wineries, a multicourse dinner and a live auction featuring exclusive travel opportunities and rare wine lots. This event benefits Benaroya Research Institute.

*When:* Aug. 21 at The Golf Club at Newcastle

*Contact:* For more information and ticket options, please visit virginiamasonfoundation.org/grapes-on-the-green.